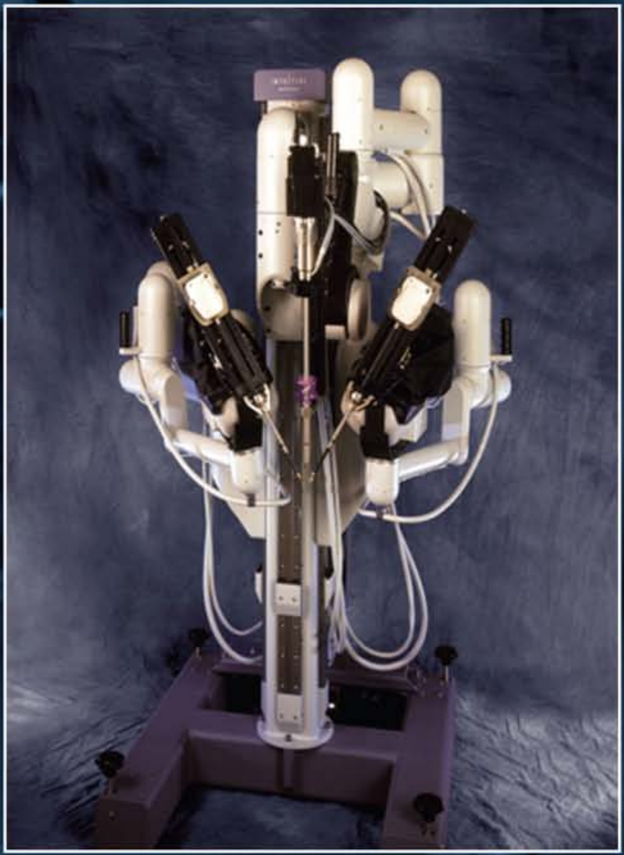
RADICAL PROSTATECTOMY:

from open to robotic



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First published in the United Kingdom in 2007 by Informa Healthcare, Telephone House, 69–77 Paul Street, London EC2A 4LQ. Informa Healthcare is a trading division of Informa UK Ltd. Registered Office: 37/41 Mortimer Street, London W1T 3JH. Registered in England and Wales number 1072954.

Tel: +44 (0)20 7017 5000
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A CIP record for this book is available from the British Library.

Library of Congress Cataloging-in-Publication Data

Data available on application

ISBN-10: 1 84184 627 9
ISBN-13: 978 1 84184 627 9

Distributed in North and South America by

Taylor & Francis
6000 Broken Sound Parkway, NW, (Suite 300)
Boca Raton, FL 33487, USA

Within Continental USA
Tel: 1 (800) 272 7737; Fax: 1 (800) 374 3401
Outside Continental USA
Tel: (561) 994 0555; Fax: (561) 361 6018
Email: *orders@crcpress.com*

Distributed in the rest of the world by
Thomson Publishing Services
Cheriton House
North Way
Andover, Hampshire SP10 5BE, UK
Tel: +44 (0)1264 332424
Email: tps.tandfsalesorder@thomson.com

Composition by CEPHA Imaging Pvt. Ltd., Bangalore, India

Printed and bound in India by Replika Press Pvt. Ltd

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Foreword

Radical prostatectomy is a gold standard for the treatment of clinically localized carcinoma of the prostate. The procedure has evolved over the last 130 years from reports of Kocher and Billroth at the end of the 19th century to Young's report in the early 20th century of a perineal approach through Millin's description of a retropubic approach in the mid-century. This was followed by a rapid acceleration of effort and expertise beginning in the 1970s with Walsh's development of and emphasis on an anatomic approach to the procedure. The advent of prostate-specific antigen (PSA) testing gave more surgeons more patients to treat, with the result that many groups and individuals from around the world have contributed to improvements in the operation, resulting in better patient care and outcomes. Large databases have enabled us to make more accurate predictions about disease status and thereby to better select patients for surgery. Still, the complication rate was higher than most would have liked and the outcomes were not as consistently good as could be hoped for. Opportunities existed for improvements in prevention and treatment of both urinary incontinence and erectile dysfunction.

The advent of laparoscopic approaches to a variety of procedures led to the inevitable application of these techniques to radical prostatectomy. After initial reports questioned the feasibility of the procedure, several of our European colleagues (including Gaston, Abbou, Guillonneau, Vallancien, and Rasweiller, among others) had the ingenuity and technical expertise to devise a successful approach to the laparoscopic radical prostatectomy. The technical expertise to perform this procedure was not easily achieved, especially by established and experienced prostate cancer surgeons who performed the procedure using open surgical techniques.

As this was occurring, the Intuitive Surgical Company received approval for use of its da Vinci surgical robot for intra-abdominal use. The system offered the reality of improved three-dimensional vision for the surgeon in a laparoscopic environment and wristed technology at the instrument tips to allow for easier suturing and dissection for a surgeon more accustomed to working in an open surgical field.

Our team at the Vattikuti Urology Institute entered the field at this time during a kind of 'perfect storm'. An established technique that had the possibility for some improvement existed, and a new but difficult to master technique that offered some hope for improvement had been developed. These were coupled with a new but untested technology and a team and individual (with the very necessary financial backing) that sought to test the application of the new technology. This resulted in our pursuit of the robotic-assisted laparoscopic approach to radical prostatectomy, or (as we prefer to call it) the Vattikuti Institute Prostatectomy, or

VIP procedure. It is also known as the da Vinci prostatectomy, or dVP.

A journey from a zone of comfort with an established technique to a new technique is both hard and exciting for surgeons. It is a voyage of discovery with uncertain ends. Many such efforts may go by the wayside with little fanfare but much time and effort spent. More importantly, it is our patients who must be willing and informed partners in such endeavors. They trust us to do what is best for them. With this in mind we sought extensive mentoring from both Bertrand Guillonneau and Guy Vallancien from the Institute Mutualiste Montsoris as we embarked on our initial laparoscopic efforts and continued to rely on their expertise as we began to develop the robotic techniques. This emphasis on patient safety and proper training remain key components of our program today, even as we approach our 3000th VIP procedure.

This textbook is a timely update and covers the evolution of the techniques and highlights current controversies about whom to operate on and how best to do so. It is divided into three parts.

The first part covers important principles of prostatic and periprostatic anatomy, specimen processing, and patient selection including staging. Part 2 contains important information about patient preparation and anesthesia which are areas that are often minimized by surgeons anxious to get their patients to the operating theater to treat the cancer. Efforts at better preoperative preparation may yield better outcomes for patients on many levels.

The 3rd to 5th parts explore technical aspects of the surgery, beginning with pelvic lymph node dissection and controversies related to the proper extent of the dissection given the stage migration that has occurred as a result of PSA screening. The following chapters are by world experts in the art and technique of various open and laparoscopic types of radical prostate surgery who present their techniques and tips.

The final portion of the textbook (Part 6) covers postoperative care and recovery of the patients with emphasis on the so-called ‘trifecta’ of cancer control, continence, and erectile dysfunction.

It is clear from the information presented that excellent results can be achieved in expert hands through a variety of approaches. It is very likely that the best technique for surgical removal of the prostate is one that the surgeon doing the operation does best. However, the robotic approach offers advantages of both open and laparoscopic approaches to the patient and some occasionally underemphasized ergonomic advantages to the surgeon. It is the ascendant procedure in the USA, with the expectation that over 50% of radical prostatectomy procedures will be performed in 2007 using this approach, only 6 years after in was introduced. Robotic-assisted radical prostatectomy is becoming the new gold standard technique for surgical removal of the prostate in the USA.

The future of robotics in surgery will probably be beyond the current da Vinci system at some point, as Intuitive Surgical and other companies develop new computer-assisted surgical platforms. The use of additional three-dimensional and real-time imaging modalities intraoperatively and better instrumentation will improve the performance of the procedures by the surgeons. Better patient selection, preparation, and rehabilitation techniques will improve patient outcomes. This is an exciting time to be involved in the treatment of patients with prostate cancer.

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Preface

The winds of change are blowing through the world of surgery for prostate cancer as never before. Open radical prostatectomy, once the gold standard treatment for localized adenocarcinoma of the prostate, is increasingly being challenged by the new technologies of laparoscopy and robotics. To complicate the issue further, other minimally invasive treatment options have emerged, including high-intensity focused ultrasound (HIFU), cryotherapy, and brachytherapy. Furthermore, conformal external beam radiotherapy (EBRT) allows higher doses of radiation to be delivered with greater accuracy to the prostate. Add to that the realization that in some low-risk cases treatment is unnecessary, and instead active surveillance may be the best option, and one can clearly see that there has never been a better time to review critically and in detail the art and science of prostate cancer surgery.

Many urologists believe that surgical removal of the prostate constitutes the best way to extirpate the malignancy and to resolve bladder outflow obstruction, but the issue of 'collateral damage' to continence and erectile function has become a major issue. The argument now between the various proponents of the different forms of radical prostatectomy encompassed in this book is not so much about cancer clearance rates, which are all excellent, but in longer-term outcomes of continence, and especially sexual function. In the final analysis, only carefully controlled and objective trials will provide us with the data we need to resolve this contentious issue.

In this book we have enlisted the world's leading experts to relate their own, very personal experiences of open, laparoscopic and robotically assisted radical prostatectomy, and the transition between them. We have also covered pre- and postoperative issues. We are most grateful to all of them for their hard work, timely manuscripts, and outstanding contributions. We would also like to thank the editorial and production staff at Informa, who have worked so tirelessly to make this book possible. State-of-the-art information on radical prostate surgery is presented here, and we leave it to the reader, and to each and every one of their patients, to decide for themselves the best way forward for them.

Roger Kirby
Francesco Montorsi
Paolo Gontero
Joseph A Smith Jr

Part 1: General considerations

CHAPTER 1

Surgical anatomy of the prostate

John G Calleary, Stella RG Smith, and Mark R Feneley

INTRODUCTION

This is the first of two chapters on anatomical features of the prostate. The second chapter concerns itself with the neurovascular bundles, pelvic fascial layers, and the external sphincter. This chapter describes topographical anatomy of the prostate in relation to surgical practice and anatomic characteristics of the normal gland as applied to clinical imaging.

TOPOGRAPHICAL ANATOMY

The prostate is a fibromuscular and glandular ‘encapsulated’ organ which lies deep in the pelvis and its shape resembles an inverted cone or walnut (Figure 1.1). The average volume in a young man is approximately 20 ml with dimensions of 3 cm (apex to base), 2.5 cm (AP distance) and 4 cm (max transverse diameter).[1] It is fixed superiorly to the bladder and inferiorly by the external urinary sphincter and membranous urethra. The apex refers to its inferior limit, and the base is the most posterior and superior portion of the gland. The prostate has four surfaces, two inferolateral, a posterior, and an anterior. The inferolateral surfaces are convex in shape and related to the medial edges of levator ani muscles and their overlying fascial layer (endopelvic fascia). The flat posterior surface is separated from the rectum by Denonvilliers’ (rectovesical) fascia and is palpable on rectal examination.[2] Denonvilliers’ fascia lies between the anterior rectal wall and the posterior surface of the prostate and seminal vesicles. It extends laterally to the fascia surrounding the neurovascular bundles. This strong fascial layer is said to be derived from two layers of pelvic fascia which have fused, although microscopically this is not always evident.[3] Denonvilliers’ fascia does, however, appear to act as a barrier against the posterior spread of prostate cancer.[4] Posterosuperior to the prostate lie the seminal vesicles and ampullae of the vasa.

Importantly in the context of radical retropubic prostatectomy (RRP), the prostate capsule is separated from the levator fascia by arteries and nerves continuing to the corpora cavernosa and also supplying the prostate. In a nerve-sparing procedure these nerves and arteries are released from the prostate by dissection of the levator fascia.[5] The anterior surface of the prostate is rounded and lies behind the pubic symphysis and connected to it by the puboprostatic ligaments. The potential space between the two is referred to as the cave of Retzius, containing adipose tissue, the superficial dorsal

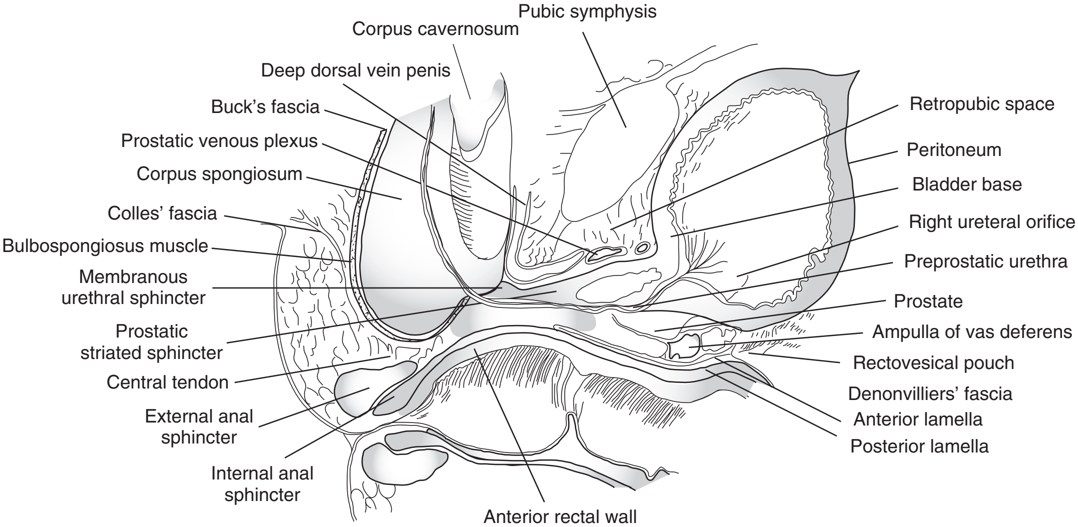

Figure 1.1 Sagittal section showing the anatomical relations of the prostate.

vein, and Santorini's venous plexus.[6] The communication between this venous plexus and the vertebral plexus is the postulated route for seeding vertebral metastases in prostate cancer.[7] The retropubic space, opened in the initial stages of RRP, may also contain aberrant vessels supplying the corpora cavernosa.

The base of the prostate is intimately related to the bladder, in continuity with the urethra and detrusor muscle. The circular smooth muscle of the bladder neck may extend into the prostate as far as the level of the verumontanum and is known as the preprostatic sphincter. The 'bundle of Heiss'[8] represents fibers of longitudinal muscle originating from the detrusor muscle laterally, that course anteriorly over the prostatovesical junction behind the 'detrusor apron'. The 'detrusor apron' is a continuation of the outer part of the anterior longitudinal smooth muscle that extends from the bladder neck over the anterior surface of the prostate.[9] It merges with the smooth muscle of the prostate at the prostatovesical junction. Fibers from the detrusor apron and prostatic smooth muscle provide the smooth muscle component of the puboprostatic ligaments. The puboprostatic ligaments are condensations of pelvic fascia, including smooth muscle, extending from the prostatic capsule at the apex to the periosteum of the pubic bones each side of the midline. A further condensation of fascia joins both ligaments across the midline. The ligaments are continuous on their deep aspect with the pubourethral ligaments. The prostatic apex and external sphincter are classically described as distinct entities but can overlap. This must be appreciated during RRP in order to avoid striated sphincteric injury, thus causing urinary incontinence.[10] The details of this relationship are covered in Chapter 2.

The prostate is traversed by the ejaculatory ducts and the urethra. The ejaculatory ducts are paired structures, formed by the conjunction of the vas deferens and the duct of the seminal vesicle. They enter the prostate on the upper part of the posterior surface and travel inferomedially within the gland. They enter the prostatic urethra on the colliculus (verumontanum), either side of the prostatic utricle. The opening has no sphincter mechanism, and lies approximately at the midpoint of the prostatic urethra. The prostatic urethra, itself, begins at the bladder neck and ends as it passes through the pelvic floor to become the membranous urethra. It is approximately 3 cm long and travels in a convex curve to exit the prostate anterosuperiorly to the apex. The verumontanum is the largest part of the urethral crest, present only in the prostatic urethra.[2] Either side of the crest lies the prostatic sinus into which the prostatic ducts open.[11] The utricle represents the remnant of the paramesonephric ducts and extends for up to 1 cm in a posterosuperior direction.[2]

RELATED STRUCTURES

Seminal vesicles

The seminal vesicles are paired structures lying superolateral to the prostate. They separate the posterior wall of the bladder from Denonvilliers' fascia. Each is composed of a sacculated tube (diameter ~ 3 mm) of some 15 cm folded back on itself so that it appears wedge shaped. Each drains via a medially placed duct, which together with the vas deferens forms the ejaculatory duct. Its blood supply is from the superior vesical artery. The tip of the seminal vesicle represents a surgically important landmark for the pelvic plexus.

The terminal vas deferens

The vas is dilated in its terminal part (ampulla) and is capable of storing sperm. It lies medial to the seminal vesicles. It joins the duct of the seminal vesicle to form the ejaculatory duct. Its vascular supply is as for the seminal vesicles.

HISTOLOGY

The prostate contains glandular and stromal tissue. In a young man the ratio is 2:1 (stromal to glandular) but changes with age and the pattern of tissue hyperplasia. Condensations of the fibromuscular stroma form the 'capsule' which covers the entire gland apart from the apical urethra and the entry point of the ejaculatory ducts. The 'capsule' is approximately 0.5 cm thick and thickest laterally. Septations from it divide the gland into lobules, each of which contains glandular tissue.[12,13] The stroma consists of smooth muscle, collagen, and elastin. There are 20–30 tubuloalveolar glands whose ducts empty into the prostatic sinus. The alveoli are branched.[12] The epithelium is formed from two cell layers, a basal layer upon which lies a secretory layer.[14] Another less numerous, cell type present within the gland and duct epithelium are the neuroendocrine cells. They are most commonly seen in the periurethral ducts and verumontanum.[15] Table 1.1 illustrates the zonal location of the glandular tissue. The prostatic urethra is lined by urothelium, in continuity with the adjacent bladder and urethra.

ZONAL ANATOMY

Since the Middle Ages, there have been many attempts to define intraprostatic anatomy. The earliest 'modern' anatomical description was by Lowsley in 1912.[16] He described five lobes – a posterior, two lateral, an anterior, and a middle – based on human fetal studies. This arrangement appeared to fit with clinical findings but could not be demonstrated in normal adult prostate. Further fine descriptions were offered by Gil Vernet,[17] and in 1968, John E McNeal proposed the now-accepted classification of zonal anatomy based on microscopic gland and duct structure[18] (Figure 1.2).

Table 1.1 Zonal distribution of glandular tissue[30]

Zone	*Total glandular tissue (%)*	*Involvement in prostate cancer (%)*
Periurethral	<1	0
Transition	5–10	~20
Central	25	1–5
Peripheral	70	70

The anterior fibromuscular stroma contains no glandular tissue and can account for one-third of normal prostatic weight. The peripheral zone is the only palpable part of the prostate and extends from the apex posterolaterally to the base. The central zone is wedge shaped, with its base at the bladder neck and apex at the prostatic utricle. Both the central and peripheral zones attach to the anterior fibromuscular stroma. The relative percentages of glandular tissue in the young adult prostate are illustrated in Table 1.1. Increased gland volume with age is predominantly due to increased transition and periurethral gland volume resulting from benign prostatic hyperplasia (BPH). The clinical significance of McNeal's zonal anatomy also relates to distinctions in the pathogenesis of prostatic disease, with adenocarcinomas most commonly developing in the peripheral zone.

CYSTOSCOPIC ANATOMY

Although cystoscopy does not assess the whole of the prostate gland, some conclusions regarding gland anatomy can be made. The position of the external sphincter can be identified by an inward bulging of the urethral mucosa. A more definitive landmark is the verumontanum and this forms the distal limit for transurethral

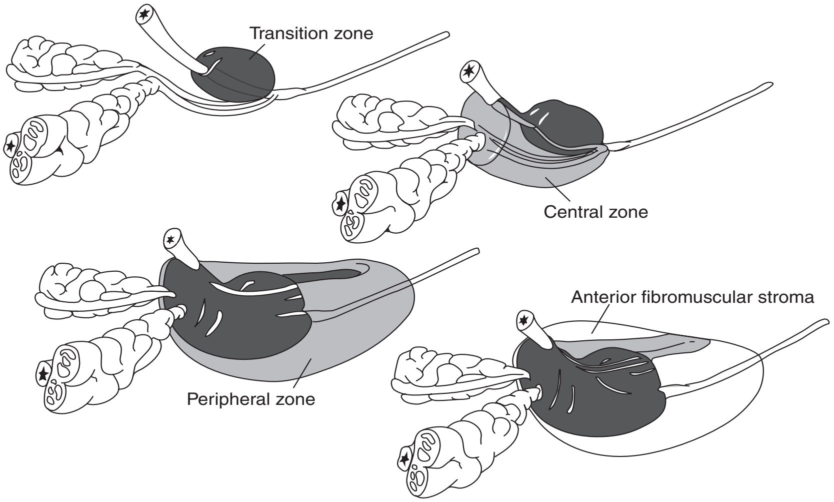

Figure 1.2 Zonal anatomy of the prostate.[19]

resection of the prostate (TURP) or bladder neck/prostatic incision (BNI). However, even this landmark can vary in its relation to the sphincter. Proximal to the verumontanum is the prostatic utricle, from which point the urethra angles upward. Normally this is 35°, but varies with the degree of BPH.[19] The so-called 'lateral lobes' refer to endoscopic appearances and represent BPH of the transition zone. The 'median lobe' represents hyperplasia of the periurethral glands.

VASCULAR SUPPLY AND VENOUS DRAINAGE

The principal arterial supply to the prostate derives from the inferior vesical branch of the anterior division of the internal iliac artery (Figure 1.3). Smaller contributions are given by the middle rectal and pudendal branches of the internal iliac. The inferior vesical artery is the second branch from the anterior division and originates near the upper margin of the greater sciatic notch. It travels forward to the bladder base, which it also supplies. It also sends branches to the seminal vesicles, including a relatively constant branch to the tip of the seminal vesicle that has some significance during radical prostatectomy. It then divides into urethral and prostatic branch groupings. The urethral branches penetrate the prostate substance at the prostatovesical junction posterolaterally. These then travel perpendicular to the urethra and approach the bladder neck mainly at the 5 and 7 o'clock positions.[2,13] These vessels then course parallel to the urethra and are named the arteries of Flocks.[20] These supply the urethra, the transition zone, and the periurethral glands, and are responsible for arterial bleeding during TURP. The capsular branch of the prostatic artery runs posterolaterally between the levator fascia and prostatic fascia. It is accompanied by the cavernous nerves and contributes to the neurovascular bundle of Walsh referred to in radical retropubic prostatectomy.[21] From this position, the neurovascular bundle approaches the prostatic apex, where it lies behind the membranous urethra. The neurovascular bundle may be tethered to the prostatic apex by fine vascular branches, and neural elements are particularly at risk of damage during dissection of the prostatic apex.[21] This arrangement is discussed in detail in Chapter 2. The capsular branch gives perpendicular branches that penetrate the capsule to supply the glandular tissue and terminate by supplying the pelvic floor with small vessels.

Venous drainage from the prostate is into Santorini's plexus. Santorini's plexus is the extremely variable venous network draining the penis and prostate.[6] From the deep dorsal vein of the penis there are three branches.

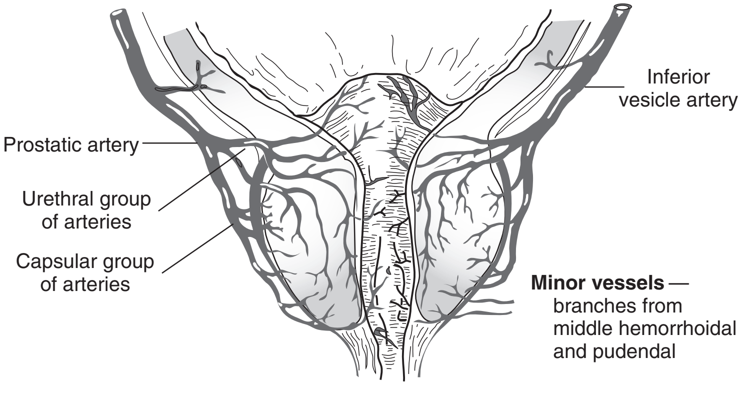
Inferior vesicle artery
Prostatic artery
Urethral group of arteries
Capsular group of arteries
Minor vessels — branches from middle hemorrhoidal and pudendal

Figure 1.3 Prostatic arterial supply and its divisions.[20]

One is superficial and runs within adipose tissue anterior to the prostate. This forms the median longitudinal vein divided when approaching the prostate within the retropubic space at radical prostatectomy or Millin prostatectomy. The other two branches are deep to the fascia and form lateral plexuses which communicate with venous plexuses around the bladder, rectum, and emissary veins of the pelvic bones. Batson proposed these as the reason for preferential metastatic spread to the pelvic skeleton.[7] Santorini's plexus drains to vesical and pudendal veins and finally to internal iliac veins. Bleeding from venous injury during surgical dissection can be significant owing to the extensive network of communicating collateral branches and their variable venous valves, but can usually be prevented or controlled by safe ligation of the deep dorsal venous complex.[22]

INNERVATION

The nerve supply to the prostate takes its course from branches of the pelvic (or inferior hypogastric) plexus that give rise to the prostatic plexus before entering the prostate itself. Fibers from the prostatic plexus either directly innervate the prostate or continue within the neurovascular bundles to the penile corpora. The pelvic plexus is located bilaterally alongside the rectum, between 5 and 11 cm from the anal verge. Its midpoint is said to lie at the tip of the seminal vesicle.[21] Branches to the prostate are intimately related to its arterial supply and entry of the ejaculatory ducts into the prostate gland. The intraprostatic innervation is discussed further in Chapter 2.

The predominant efferent innervation is sympathetic, with preganglionic sympathetic fibers (T10 to L2) passing via the hypogastric nerve to the pelvic and prostatic plexus.[23] Parasympathetic preganglionic fibers (S2–4) travel from the intermediolateral column of the sacral cord via the pelvic nervi erigentes. From there they synapse with postganglionic cells on the capsule or with intraprostatic stroma.[23] Afferents from the prostate are carried by the pelvic and hypogastric nerves to the sacral cord (perineal afferents) and thoracolumbar cord (suprapubic and groin), respectively. Pacinian corpuscles are present only in the capsule of the adult prostate. The function of the sympathetic efferent supply is predominantly in capsular and contraction of stromal smooth muscle. The exact parasympathetic function is unclear.[23]

LYMPHATIC DRAINAGE

The majority of lymphatics drain into a periprostatic subcapsular plexus. This plexus drains primarily through obturator nodes to the internal and common iliac nodes. However, some drainage also occurs to the presacral and external iliac lymphatics.[24] The obturator nodes are found in a triangle located between the inferior border of the external iliac vein, the femoral canal, and the obturator nerve, with its apex at the bifurcation of the common iliac artery.[21] A full discussion of lymphatic drainage and lymph node dissection is given in Chapter 8.

PROSTATE ANATOMY APPLIED TO CLINICAL IMAGING

Ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) are used in clinical practice for structural imaging of the prostate. The anatomy of the normal prostate as applied to imaging with these modalities will be described; imaging of prostatic disease is beyond the scope of this chapter (see Chapter 6).

Ultrasound

Transabdominal ultrasound is of limited value in defining intraprostatic and periprostatic anatomy. Transrectal ultrasound (TRUS) provides superior imaging characteristics and has important clinical applications. TRUS is used for estimating prostate volume, for which it is more reliable than transabdominal scanning. It is routinely used in the diagnosis of prostate cancer for guiding needle biopsy. It can also be used to guide therapy (e.g. cryotherapy) and as a therapeutic modality in itself (e.g. high-intensity focused ultrasound [HIFU]). TRUS allows the array to be placed in close proximity to the prostate for imaging with higher frequencies (6–10 MHz) that give better anatomical definition. Gray-scale imaging is usually done in two planes, although 3D reconstruction of the prostate is possible.[25] The intraprostatic zones described by McNeal are only partially distinguished on ultrasound. Nevertheless two distinct regions can be seen: the ‘inner’ gland and ‘outer’ gland. The ‘inner’ gland includes the transition zone and periurethral glands (Figure 1.4). The ‘outer’ gland comprises the peripheral and central zones.[26] The course of the urethra is also readily evaluated, especially when periurethral contrast (aerated anesthetic gel) is used. Likewise, the ejaculatory ducts are identifiable. The capsule is difficult to visualize and its involvement in prostate carcinoma relies on loss of contour of the gland surface and/or loss of the periprostatic fat signal.

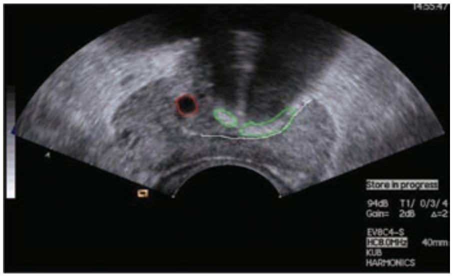

Figure 1.4 Transrectal ultrasound transverse image showing ‘outer’ and ‘inner’ gland. The red circle outlines a prostatic cyst. The green lines outline calcification. The white line shows demarcation between the inner (above and central) and outer (below and peripheral) gland. Subsequent biopsy demonstrated adenocarcinoma on the right side.

The apex is identifiable by following the gland contour inferiorly, usually in the sagittal plane. The striated sphincter is seen as a hypoechoic area just distal to the apex, but the ease with which it is identified depends on the degree of apex–sphincter overlap. The base can be difficult to visualize if the bladder is empty. The neurovascular bundles are identified by their posterolateral position and by using color and/or power Doppler.

The ultrasonographic anatomy, as described in the preceding paragraph, is also visualized using the lower-frequency (3–4 MHz) probes used in visually directed HIFU. This technique, incorporates ultrasound as a treatment modality for prostatic disease, as well as virtual real-time imaging.[27]

Computed tomography

Computed tomography is not usually useful for imaging prostatic anatomy unless contrast enhancement is used.[28] CT can be worthwhile however for evaluating nodal and soft tissue metastases. The lateral borders of the prostate are delineated by the surrounding adipose tissue between the gland and the levator muscles of lower signal intensity, but this does not reliably identify microscopic extraprostatic invasion by malignant disease.

Magnetic resonance imaging

Magnetic resonance imaging represents the best modality for depiction of prostatic anatomy (Figures 1.5–1.7). The normal prostate is indistinguishable from the seminal vesicles, veins, and neurovascular bundles using a T1-weighted sequence: all have a low signal which is close to that of skeletal muscle. The T1-weighted image is good for imaging lymph nodes, which appear as low-signal areas in the high-signal adipose tissue. It detects biopsy-induced changes. T2-weighted imaging is useful for intraprostatic anatomical detail. The peripheral zone in a normal prostate demonstrates a

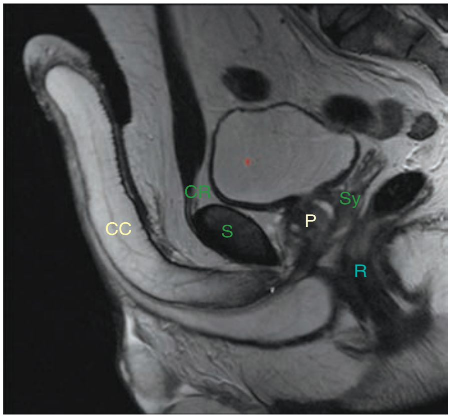

Figure 1.5 T2-weighted sagittal image showing normal prostate and its relations: B = bladder; CR = cave of Retzius; SV = seminal vesicle, S = pubic symphysis, CC = corpus cavernosum, P = prostate, R = rectum, U = urethra.

homogenously high signal which is less than fat but greater than muscle. The central and transition zones have high signals but lower than that of the peripheral zone. The former two are indistinguishable on the basis of imaging. As could be anticipated, the fibromuscular stroma shows low signal. The seminal vesicles demonstrate high signal intensity. The capsule can be identified as a lower-signal-intensity area around the peripheral zone and the neurovascular bundles as low-signal-intensity areas posterolateral to the prostate.[29]

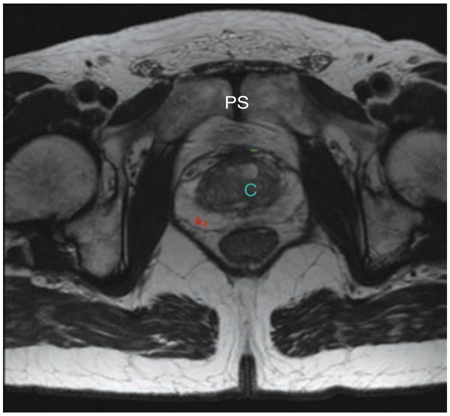

Figure 1.6 T2 transverse image of prostate: PS = pubic symphysis, Per Z= peripheral zone of prostate, C = central and transition zones, green line signifies position of venous plexus.

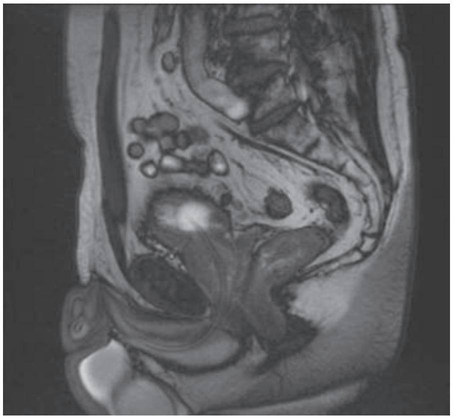

Figure 1.7 Sagittal MRI image demonstrating the course of the urethra (by an indwelling urinary catheter) in a man with extensive adenocarcinoma of the prostate.

CONCLUSION

Many elegant studies contribute to current appreciation of prostatic anatomy, including the zonal intraprostatic architecture, and its relation to prostatic disease, venous anatomy, and the neurovascular bundles necessary for penile erection. This knowledge has empowered surgeons performing radical prostatectomy to obtain excellent functional outcomes without sacrificing oncological control.

ACKNOWLEDGMENT

We thank Dr Clare Allen, Consultany in Uroradiology, University College London Hospitals NHS Foundation Trust, London, UK for supplying the radiological illustrations.

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CHAPTER 2

Cadaveric anatomy of structures related to the prostate

Paolo Gontero, Giansilvio Marchioro, Gloria Maso,
Alessandro Tizzani, and Bruno Frea

INTRODUCTION

The surgical anatomy of the prostate and its related structures has been refined in relatively recent years, enabling the popularization of radical prostatectomy as a routine procedure in everyday urological practice. A precise knowledge of the topographic anatomy of the dorsal vein complex, the urethral sphincteric complex, the neurovascular bundles, and the periprostatic fasciae has allowed a considerable reduction in blood loss, excellent continence, and potency rates with good cancer control. In spite of these achievements, some controversies exist as regard the anatomical details of certain structures. The number of layers of Denonvilliers' fascia is still a matter of debate as are the type of structures forming the sphincteric mechanism and the shape of the rhabdosphincter. On the other hand, a precise knowledge of the topographic location of the pelvic plexus and the neurovascular bundles, the possible variations in the course of the deep dorsal vein branches, or the occurrence of pudendal accessory vessels may help the surgeon to improve both the oncological and the functional results of the procedure.

The aim of the present study, out of a detailed description of the prostatic surgical anatomy, is to discuss some controversial topics related to the prostatic loggia anatomy in the light of cadaveric images showing details usually not easily recognized while performing live surgery.

PUBOPROSTATIC COMPLEX

Dissection in the retropubic space during radical prostatectomy carries a serious risk of bleeding, which can be prevented by a precise knowledge of the anatomy of the dorsal vein complex.

According to the anatomical studies recently conducted by Wimpissinger et al[1] in the 'puboprostatic complex', the following elements can be recognized: (1) the puboprostatic ligaments, (2) the dorsal vein complex, and (3) fibromuscular and soft connective tissue.

1. *The puboprostatic ligaments* are pyramidal structures comprising a thickening of the medial part of the endopelvic fascia that inserts distally into the periosteum of the pubis symphysis. The proximal portion continues with muscle fibers of

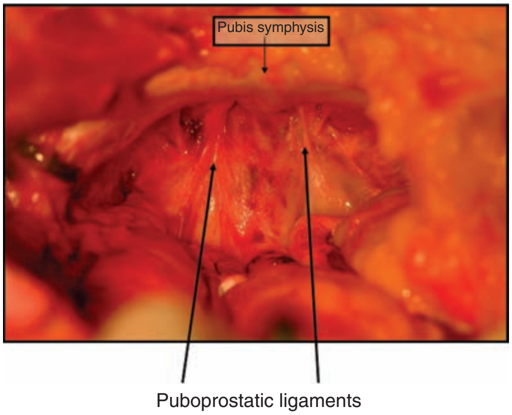

Figure 2.1 The puboprostatic ligaments.

the bladder wall. In this way they contribute to the formation of a structure named the 'detrusor apron', which represents a direct continuity of the anterior bladder wall covering the ventral face of the prostate.[2] Figure 2.1 shows the two distal portions of the ligaments that usually present in adults, with a width of 4–5 mm, and forming a 2 mm hiatus.[3]

2. *The dorsal vein complex* comprises the deep dorsal vein of the penis entering the retropubic space through Buck's fascia below the pubic arch into three major branches: one superficial branch and two (one on the right and one on the left) lateral venous plexuses.[4] The superficial branch is formed of one or more veins that have perforated through the pelvic fascia just behind the posterior pubic wall, lying within the adipose tissue that covers the 'detrusor apron' and usually entering the vesicovenous plexus by re-entering the pelvic fascia proximal to the prostatovesical junction. Several anatomical variations of these superficial preprostatic veins have been reported by Myers.[5] Although the most common finding (in nearly 60% of cases) is a single midline vein, in another 20% of cases there is a bifurcation that originates right or left pelvic sidewall branches. The third most common distribution is a single vein to the pelvic sidewall without vesicovenous plexus anastomosis and, finally, in about 10% of cases the vein is completely absent. The lateral venous plexuses (popularly known as Santorini's plexus) form a network of veins lying immediately underneath the puboprostatic ligaments and the endopelvic fascia. While traversing posterolaterally, they usually originate branches that communicate with pudendal, obturator, and vesical plexuses. Near the puboprostatic ligaments, small branches may penetrate the pelvic sidewall musculature and communicate with the internal pudendal veins. In Figure 2.2 the deep dorsal vein of the penis can be seen (after removal of the pubis bone), branching into two veins that form the lateral venous plexuses. An increased number of branches, as shown in Figure 2.3, as well as anatomical variations in the veins' course are frequent also at the deep venous plexus level and may account for the unpredictable and sometimes unavoidable troublesome bleeding during radical prostatectomy.

3. *Fibromuscular and soft connective tissue* separate the Santorini's plexus from the prostate and attach the prostate to the pubic arch in the median plane inferior to the puboprostatic ligaments. This attachment, named the 'intermediate pubourethral ligament',[6] inserts to the anterior commissure of the prostate, also integrating some veins in the suspension. The intermediate pubourethral ligament and the two puboprostatic ligaments together constitute a T-shaped attachment to the pubic arch, with the first forming the vertical plane and the latter the horizontal one.

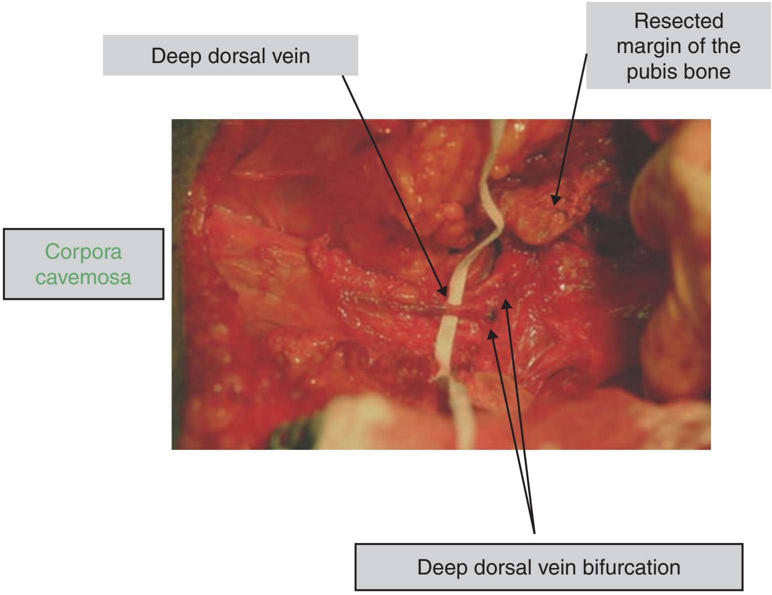
Deep dorsal vein
Resected margin of the pubis bone
Corpora cavemosa
Deep dorsal vein bifurcation

Figure 2.2 The deep dorsal vein of the penis.

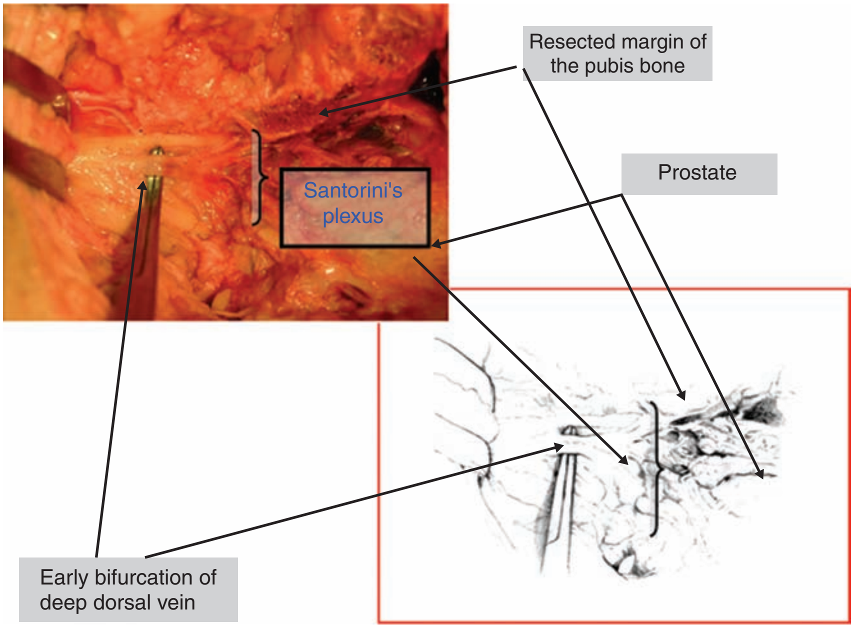
Resected margin of the pubis bone
Prostate
Santorini's plexus
Early bifurcation of deep dorsal vein

Figure 2.3 Branches of the deep dorsal vein.

All these structures, the puboprostatic ligaments with the detrusor apron and the superficial preprostatic veins superiorly and the Santorini's plexus and the intermediate pubourethral ligament inferiorly, are usually encountered before exposing the prostate apex during a retropubic approach to radical prostatectomy.

NEUROVASCULAR BUNDLES AND THE PELVIC PLEXUS

A precise knowledge of the neurovascular anatomy of the prostate is an essential prerequisite for a nerve-sparing approach to radical retropubic prostatectomy. This has been excellently refined in cadaveric studies by Walsh and co-workers.[7,8]

The neurovascular bundles that course posterolateral to the prostate consist of a complex structure related to the vascularization of the outer prostatic portion and to the innervation of prostate, urethra, and corpora cavernosa. Small arterial branches originating from the inferior vesical artery and venous vessels draining in the homonymous vein constitute the vascular portion of the bundles. They run in the lateral pelvic fascia, medially to the cavernosal nerve branches (vide infra) to terminate as capsular vessels that pierce the prostatic fascia. These vessels are important when performing a nerve-sparing radical retropubic prostatectomy, as they provide the landmark for the identification of the nerves.

The pelvic plexus is a retroperitoneal structure located on the lateral wall of the rectum (Figure 2.4). The mid-caudal portion of the pelvic plexus is located at the tip of the seminal vesicles (Figure 2.5) and emanates autonomic fibers, which form a dense network with the described vessels.[9–11] Some of them perforate the prostatic capsule to enter the substance of the prostatic gland. These branches are inevitably sacrificed during a nerve-sparing approach,

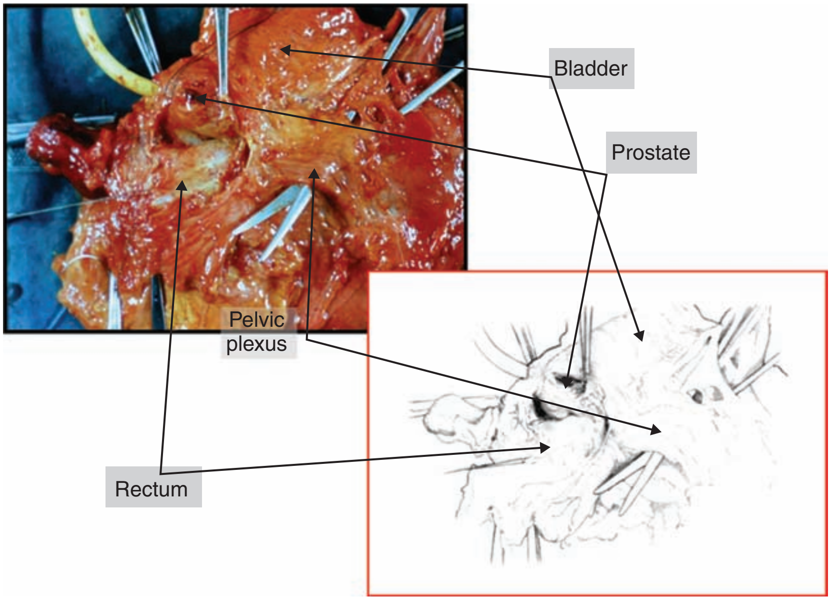

Figure 2.4 The pelvic plexus.

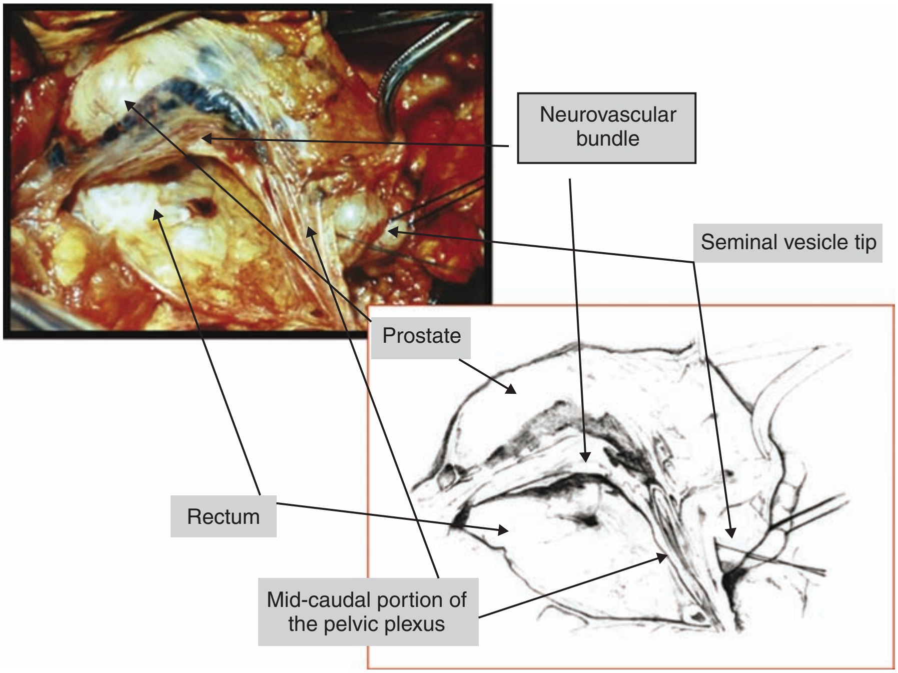

Figure 2.5 Mid-caudal portion of he pelvic plexus.

but it is believed that they do not contribute significantly to erectile function. The majority of nerve fibers, known as the cavernous branches, travel in a direct route from the pelvic plexus toward the posterolateral base of the prostate, gradually coalescing from a group of fibers approximately 12 mm wide to a more organized bundle approximately 6 mm wide at the level of the prostate. At this point, they lay just underneath the lateral pelvic fascia, between the levator fascia and the prostatic fascia (a fibrous layer in direct continuity with the true prostatic capsule). In Figure 2.6 a prominent neurovascular bundle has been detached from the posterolateral aspect of the apex, mid portion, and base of the prostate. At the level of the membranous urethra, the cavernous nerves are located at the 3 o'clock and 9 o'clock position, just beneath the striated sphincter (that at this point surrounds both the urethra and the prostatic apex) (Figure 2.7).

DENONVILLIERS' FASCIA

Denonvilliers' fascia, a surgical landmark for any urologist performing radical prostatectomy, has been and still is a matter of debate regarding its embryological origin and the number of layers that form its structure. We report the description given by Charles Denonvilliers himself in 1836:

> *'Behind the prostate, between the seminal vesicles and the rectum, there is a distinct membranous layer, which I call prostatoperitoneal. This is its position: from the 2 sides it fuses with the compact cellular tissue which surrounds the venous plexus at the base of the bladder; on the anterior side it runs to the far side of the prostate; on the posterior side it adheres to the part of the peritoneum that descends between the bladder and the rectum.... The lower surface which touches the rectum barely adheres to it by a very loose cellular tissue...'*
>
> Denonvilliers[12]

The presence of two layers (a thick posterior and a thin anterior layer), first postulated by

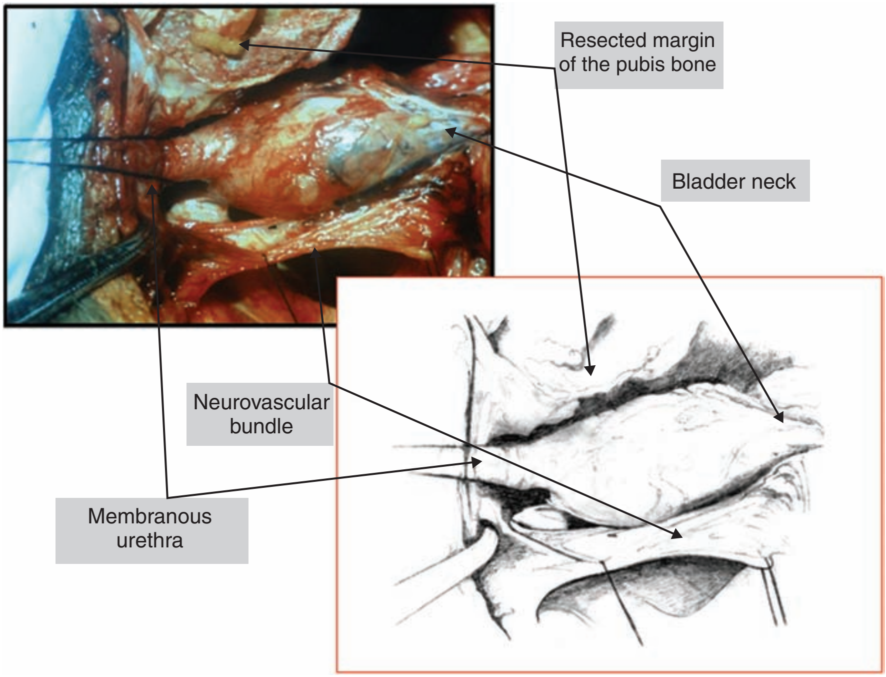

Figure 2.6 Neurovascular bundle.

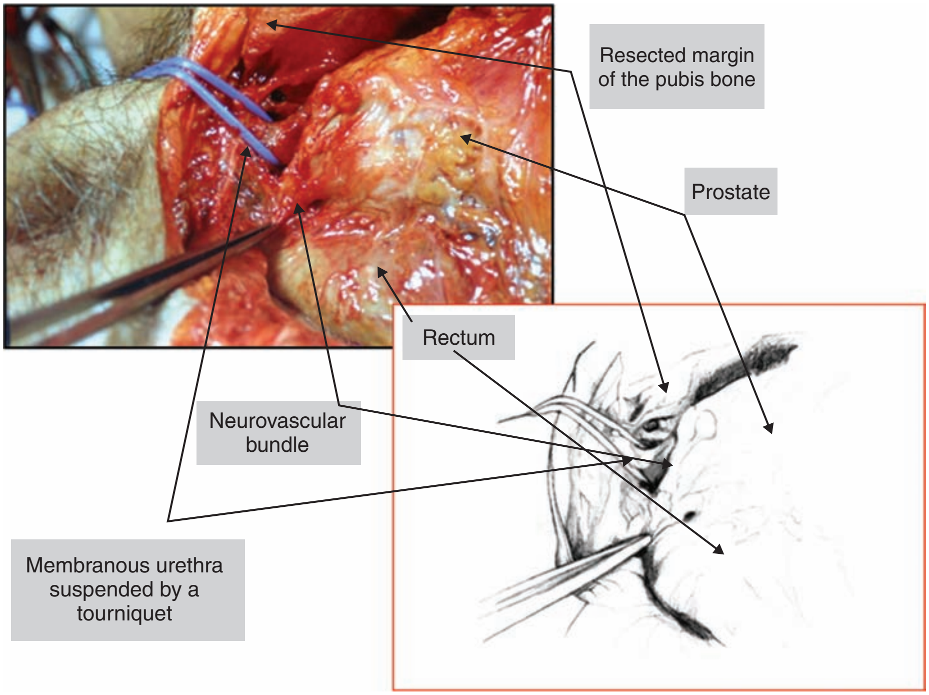
Resected margin of the pubis bone
Prostate
Rectum
Neurovascular bundle
Membranous urethra suspended by a tourniquet

Figure 2.7 Neurovascular bundle: cavernous nerves.

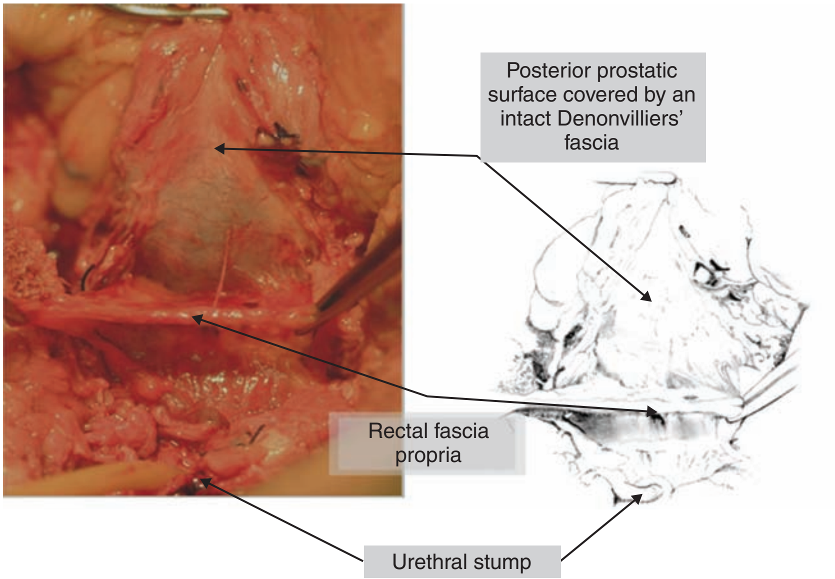
Posterior prostatic surface covered by an intact Denonvilliers' fascia
Rectal fascia propria
Urethral stump

Figure 2.8 Rectal fascia propria.

Smith in 1908[13] as a result of the origin of the fascia from the fusion of the pelvic portion of the embryonal peritoneum, was further elucidated by Tobin and Benjamin.[14] They described, between the bladder and the rectum, a middle peritoneum layer lying between two mesenchymal layers covering the posterior bladder wall and the anterior rectal surface. They postulated Denonvilliers' fascia originating from the anterior mesenchymal layer as well as from a fibrous membrane left behind from the receded middle peritoneal layer. According to these authors, from the prerectal mesenchymal layer developed the rectal fascia propria, which, although not technically correct, could be designated as the posterior layer of Denonvilliers' fascia. Recently, after a thorough review of the literature, van Ophoven and Roth[15] suggested that Denonvilliers' fascia consists of a single layer arising from the fusion of the two walls of the embryological peritoneal cul-de-sac and that the histologically evident double-layered quality is not distinguishable intraoperatively. Additionally, they conclude the so-called 'posterior layer' described by some researchers is in fact the rectal fascia propria. Figure 2.8 shows the rectal fascia propria, which is well defined from Denonvilliers' fascia covering the posterior prostatic surface and the seminal vesicles. As shown in Figure 2.9, the Denonvilliers' fascia can be easily split intraoperatively into two layers, a thick posterior fascia and a thin anterior fascia.

URETHRAL SPHINCTERIC COMPLEX

Based on the different ontogeny of the sphincteric muscles, the sphincteric complex has been divided into two compartments: the first, described as the inner smooth muscle layer in the proximal urethra, is an extension of the detrusor muscle; the second is represented by the external striated sphincter muscle.[16] A single-unit system origin of the urethral sphincter from the bladder detrusor muscle has

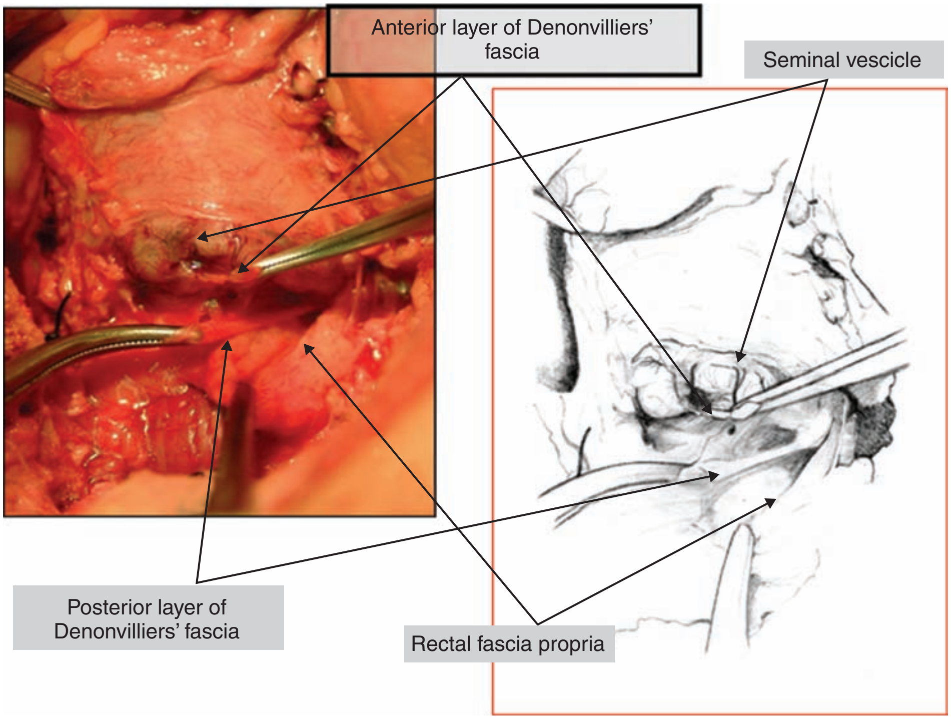
Anterior layer of Denonvilliers' fascia
Seminal vescicle
Posterior layer of Denonvilliers' fascia
Rectal fascia propria

Figure 2.9 Denonvilliers' fascia: anterior and posterior layers.

also been hypothesized.[17] In their recent anatomical study on human fetuses of different gestational ages, Yucel and Baskin[18] favored an independent origin of the continence mechanism from three different muscular structures – the detrusor, the trigone, and the urethral sphincter.

According to the macroscopic appearance, three main components can be recognized in the urethral sphincteric complex: (1) the prostatomembranous urethra, (2) a periurethral musculature known as the rhabdosphincter, and (3) extrinsic paraurethral musculature and connective tissue structures of the pelvis. The complex is surrounded by the prostatic apex proximally, the bulb of the corpus spongiosum distally, the dorsal vein complex ventrally, the rectum dorsally, and the levator ani musculature laterally.

1. The prostatomembranous urethra (in its cranial part) contains the so-called internal sphincter, which is located at the bladder neck and is anatomically defined as a base plate consisting of ventral lamellas of the bladder musculature and dorsal trigonal musculature.[19] The trigonal musculature extends caudally, narrowing to the verumontanum. The outer longitudinal muscle layer of the bladder wall surrounds the above-mentioned muscular structures of the prostatomembranous urethra by continuing ventrally from the circular muscle fibers of the bladder neck down to the level of the verumontanum. Dorsally, the outer longitudinal layer of the detrusor attenuates beneath the trigone before reaching the prostate.[18]

2. Figure 2.10 shows the macroscopic appearance of the rhabdosphincter as a concentric muscular structure surrounding the membranous urethra distal to the prostatic apex after removal of the pubis bone. Controversy exists in the literature regarding the exact

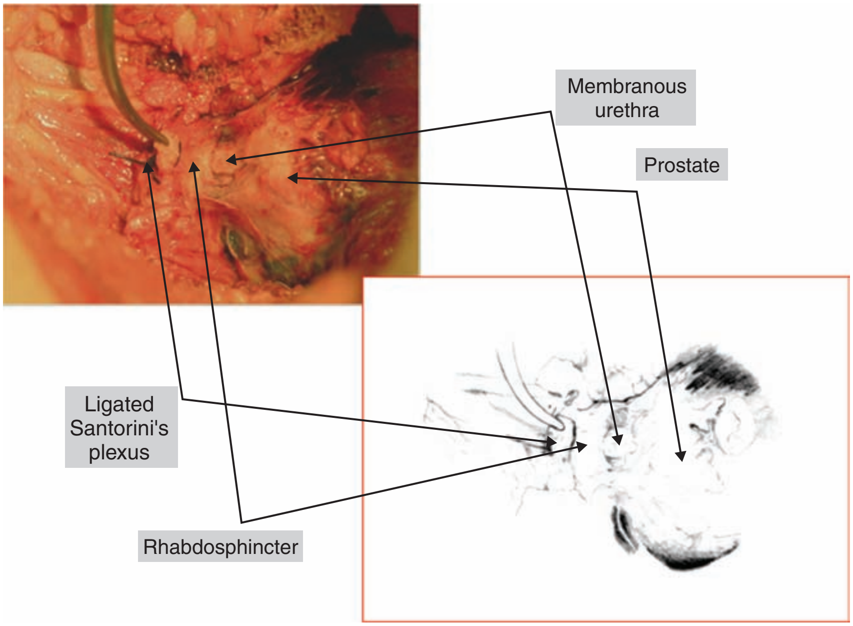

Figure 2.10 The rhabdosphincter.

rhabdosphincter configuration. Some authors suggest that the muscle has an inverted horseshoe or omega sign arrangement, with minimal or even incomplete development of the muscle dorsally.[5,20] According to Yucel and Baskin,[18] the external sphincter extends on the ventral surface of the prostate from the prostatic base to the membranous urethra in the form of a crescent shape above the verumontanum and a horseshoe shape below the verumontanum. These authors believe that the dorsal wall of the sphincter mechanism is mainly formed by the trigone, which prevents the external sphincter muscle fibers extending dorsally. Dorschner et al[21] have identified connective tissue filling the dorsal area of the external sphincter that is not completely closed.

Similar to our observation, others identify the rhabdosphincter as a concentric musculature surrounding the prostatomembranous urethra. In their study on frozen sections of six cadaveric pelves, Burnett and Mostwin[22] found that the muscle thickness was similar ventrally and dorsally, with a greater thickness at each lateral extent. They also confirmed the presence of sphincteric muscle fibers in contact with the prostatomembranous urethra, extending from the base of the bladder to the perineal membrane ventrally and from the prostate to the perineal membrane dorsally, as previously suggested by Oelrich.[23]

3. Question exists whether the musculus sphincter urethrae (rhabdosphincter) is independent and easily separable from the surrounding pelvic floor muscles, as seems to be suggested in Figure 2.10, or is constituted as a unique structure within the muscle system of the pelvic floor and particularly within the so-called deep transverse perineal muscle.[24] The rhabdosphincter is contained by a fascial framework. In its ventral aspect the fascia is a caudal extension of the fascia trasversalis, entering the urogenital hiatus as it joins with the endopelvic fascia overlying the prostate and the bladder

(at the level of the pubic bone this fascia condenses to form the puboprostatic ligaments). Laterally, the endopelvic fascia fuses with the medial fascia of the levator ani musculature to form the lateral pelvic fascia bordering the prostate. The levator ani forms a thin muscular layer from the pubis to the tip of the anus in lateral relationship to the rhabdosphincter. At the apical extent of the prostate, the lateral pelvic fascia courses in a dorsolateral relationship to the prostate and merges dorsally with Denonvilliers' fascia.[22] At the immediate dorsal aspect of the urethral sphincteric complex, a grossly apparent median fibrous tissue raphe is visible, which forms a posterior insertion point for the muscular fibers of the rhabdosphincter and extends from Denonvilliers' fascia at the prostatic apex to the central tendon of the perineum. The rectourethralis muscle is usually seen to connect the dorsal part of the rhabdosphincter to this structure.[22] Classic anatomy textbooks define the deep transverse perineal muscle as the main structure dorsal to the rhabdosphincter in the urogenital diaphragm.[24] All the above-mentioned musculofascial structures provide a fixation point for the urethral sphincteric complex to the surrounding skeletal structures.

ACCESSORY PUDENDAL ARTERIES

Accessory pudendal arteries have been reported with a variable incidence (depending on the means used for their identification) and are thought to contribute significantly to penile vascularization in adjunct to the internal pudendal arteries. Studies of cadaveric dissections show an incidence as high as 70%,[25] but the incidence decreases to 4% in open radical

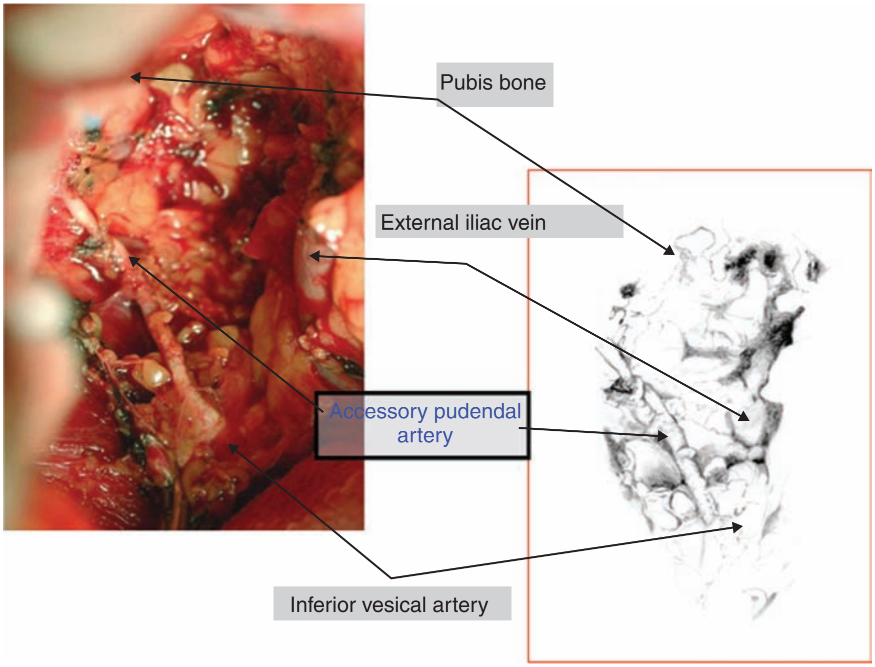

Figure 2.11 Accessory pudendal artery.

prostatectomy series.[26] A recent laparoscopic study has shown that the intraoperative incidence of accessory pudendal arteries is higher than previously reported (25%) in view of the improved magnification.[27] On cadaveric dissections, the majority of accessory pudendal arteries arise from the inferior vesical arteries (50%), followed by the obturator artery (37%).[25] Figure 2.11 shows an accessory pudendal artery arising from the inferior vesical artery. From that origin, the arteries run within the perivesical fat lateral along the prostate surface and pierce the endopelvic fascia at the level of the distal third of the gland to supply the urethral sphincter and penile vascularization. Recently, accessory pudendal arteries emerging through the levator ani muscle, near the prostate apex, have been described in 13% of a laparoscopic radical prostatectomy series.[27] Accessory pudendal arteries are thought to contribute significantly to both penile and sphincter blood supply and they may impact on postoperative potency and continence. Early recognition and intraoperative sparing techniques of these aberrant vessels are therefore suggested for improving functional results of radical prostatectomy.

CONCLUSIONS

In the present study we have reviewed some key aspects of the topographic and surgical anatomy of the prostate in relation to its surrounding organs. Through cadaveric dissection, we have attempted to show details often not easily recognized during live surgical procedures. The close relationship of the pelvic plexus with the seminal vesicles, as shown in Figure 2.5, is a reminder to pay particular attention in the dissection of the vesicles while performing nerve-sparing surgery. The debate on the number of layers of Denonvilliers' fascia should not create confusion when performing surgery for locally advanced prostate cancers. In these cases, it is important to have in mind that the whole Denonvilliers' fascia should be left attached to the prostate and the seminal vesicles, leaving out only the rectal fascia propria (shown in Figure 2.8) in order to minimize the risk of positive surgical margins. Whether it is horseshoe, omega or circular shaped, the rhabdosphincter appears in Figure 2.10 as a concentric muscular structure, well defined from the surrounding fibromuscular structures of the anterior perineum in contrast to other anatomical descriptions. Notably, following careful dissection of the prostatic apex, the membranous urethra can be pulled out of the rhabdosphincter (see Figure 2.10) and transected with minimal damage to the striated muscular ring. Finally, the anatomical variations of the dorsal vein complex (see Figures 2.2 and 2.3) should always be kept in mind in order to avoid significant bleeding during radical prostatectomy.

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CHAPTER 3

Indications for radical prostatectomy

Hein Van Poppel, Chao-Yu Hsu, and Steven Joniau

INTRODUCTION

There is no better way to cure localized prostate cancer than by radical surgical removal.[1] The surgical treatment for prostate cancer was introduced more than a century ago. It was the French surgeon R Proust who, in 1901, described the technique of perineal prostatectomy for the first time but, in most historical reviews, H Young is said to be the first to describe the procedure in 1904 at the Johns Hopkins University.[2,3] The first important series of radical prostatectomies (RPs) performed through a perineal approach was published by Turner and Belt.[4] The retropubic approach was introduced by Millin,[5] while retrograde radical retropubic prostatectomy was described in detail by Chute and a few years later by Campbell.[6,7] The procedure remained unpopular because of its morbidity, with blood loss, urinary incontinence, and impotence considered too high a price to pay for cure of a disease that often had a non-life-threatening course. The pioneering efforts of Walsh in defining the anatomy of the dorsal vein complex and neurovascular bundles led to improvement of the morbidity, which, together with the widespread application of prostate-specific antigen (PSA) testing, resulted in the popularization of radical prostatectomy.[8] More recently, laparoscopic radical prostatectomy (eventually robot assisted) is being routinely performed in expert centers but its possible advantages for the patient in terms of oncological and functional results are not yet established.

In men with localized prostate cancer and a life expectancy of 10 years or more, the goal of management is to eradicate the disease. Watchful waiting, nowadays called active monitoring, can be advocated in elder patients with a shorter life expectancy with low-stage and low-grade disease. Primary hormonal treatment can be given in patients with localized prostate cancer when they are not suitable candidates for more aggressive treatment. Radical prostatectomy offers the best chance to eradicate clinically organ-confined cancer and selected cases with locally advanced disease. Despite the lack of randomized clinical trials, results from many individual series, pooled analyses or meta-analyses and population-based studies suggest that radical prostatectomy provides the best chance of long-term cure from early prostate cancer.[9] There should not be any difference in clinical outcome between retropubic, perineal, or laparoscopic radical prostatectomy.

Ideally, the procedure should be reserved to patients who have curable disease and who are going to live long enough to benefit from it. Therefore, case selection is an important issue.

DISEASE-RELATED INDICATIONS

Organ-confined disease

T1 tumors are clinically inapparent cancers that are not palpable at digital rectal examination or visible by imaging. At the age of 50 years, approximately 30% of men have incidental prostatic carcinoma, whereas only 1 out of 10 is at risk of developing a clinically significant cancer. Therefore, it is questionable whether every case of prostate cancer found incidentally on transurethral resection (TURP) or needle biopsy warrants aggressive treatment.

Stage T1a prostate cancer

Stage T1a prostate cancer, an incidental finding at TURP, involves 5% or less of tissue resected,[10] whereas the stage T1b is when more than 5% of tissue contains cancer or when poorly differentiated tumor is present.

The lifetime progression rate in untreated patients with T1a tumors ranges from 16% to 36%[11] and at 5 years progression of untreated T1a prostate cancer is reported to be only 5%.

However, at longer follow-up these cancers can progress in about 50%.[12] In younger patients who are expected to survive 15 years or more, the chance of progression is therefore high enough to warrant radical prostatectomy.[13,14]

T1b tumors

For T1b tumors the situation is different, since about half of the patients are expected to have disease progression after 5 years[15] and aggressive treatment seems indicated more often.

Therefore, the distinction between T1a and T1b tumors is a relevant problem. A repeated TURP upstages only 10% of patients from a T1a to a T1b tumor, although 85% may have a residual cancer.[16] Moreover, a repeat TURP can render a radical prostatectomy more difficult because of the small amount of gland that is left and that, together with periprostatic fibrosis, makes a radical prostatectomy more difficult.[17] While a nerve-sparing radical prostatectomy should be curative for the large majority of patients with T1 cancer, a prior repeat TURP can be responsible for higher incontinence rates and make preservation of the neurovascular bundles more difficult. Therefore, when a T1a disease is diagnosed on TURP or adenomectomy, a new evaluation including systematic prostatic biopsies from the peripheral zone is preferable. If one or more biopsies are positive, the tumor is considered T1b and the patient will be a candidate for radical surgery when having a life expectancy of 10 years or more.

It was reported that radical prostatectomy provides a recognizable advantage over radiotherapy in clinical T1a-b cancers,[12] but the limited sample size does not allow this chapter to conclude that radiotherapy is not a valid option. In very small residual prostates (<10 g) a RP can be rather difficult and in these cases radiotherapy might be considered an option, certainly in elder patients.[18]

Since the introduction of PSA screening programs, prostate cancer stages T1a and T1b are becoming rare. Many urologists will perform prostate biopsies in case of any suspicion of malignancy before doing a transurethral resection or an adenomectomy, at least in patients who, when cancer is detected, might be candidates for local treatment by surgery or radiotherapy.

T1c disease

T1c disease, on the other hand, is becoming more and more prominent and nowadays constitutes the vast majority of prostate cancers treated. T1c is a non-palpable tumor identified by prostate biopsy because of an aberrant PSA. Men with a persistently suspicious PSA level or suspicious PSA evolution after initial negative biopsy should undergo at least one repeat biopsy including transition zone sampling. High-grade prostatic intraepithelial neoplasia (HG PIN) is not an indication to perform RP. In men with benign prostatic hyperplasia (BPH) and an embarrassingly high PSA level, TURP or open adenomectomy may be proposed, at least in symptomatic patients.

While careful observation was reported to be a viable option for some men with clinical stage T1c prostate cancer,[19] other experts reported that up to 84% of stage T1c prostate cancers diagnosed by PSA screening are significant tumors.[20] Most authors today agree that PSA-detected tumors are most commonly significant tumors and should not be left untreated.[21–23] Nevertheless, efforts must be undertaken to recognize beforehand those tumors that after radical prostatectomy prove to be so-called insignificant, meaning that they should not have needed RP at that given moment. Active monitoring is difficult to advocate in younger men with microscopically proven invasive adenocarcinoma of the prostate and this expectant (delaying) management policy needs to be further studied.

The 6-year biochemical PSA recurrence-free survival rate for clinical T1c after RP was reported to be 87%, whereas pathological stage was the single best prognosticator of progression.[24] Others reported that patients with clinical stage T1c cancers had a significant progression-free survival advantage compared to those with clinical stage T2b/c disease. The 5-year progression-free survival was 84%. Disease-free survival in the stage T1c group was similar to that in the clinical stages T1a to T2a group but significantly better than that in the T2b/c group.[25]

T2 disease

T2 is palpable and/or visible tumor. T2a is when the tumor involves half a lobe or less, T2b is a tumor involving more than half a lobe, but not both lobes. T2c is when both lobes are involved. It has been shown that the median time of progression to extracapsular disease in untreated stage T2 patients is about 6–10 years.[26] Therefore, radical prostatectomy is the local treatment of choice, next to radiation treatment, which is mostly reserved for older patients.

In localized prostate cancer, the patient's life expectancy, overall health status, and tumor characteristics (cancer volume and cancer grade) should be evaluated before surgery. There is a correlation between tumor volume and the risk of disease progression and an ideal cancer volume for RP was suggested to vary between 0.5 and 4 cc.[27] However, the precise preoperative estimation of tumor volume by current diagnostic tools is still insufficient. Larger tumors are more likely to perforate the prostate capsule and also poorly differentiated tumors will extend more often outside the prostatic capsule.[28] These considerations need to be taken into account when selecting patients for nerve-sparing RP. It is wise to resect the neurovascular bundle when multiple biopsies are positive on one side or when a Gleason grade 4 or 5 is present.

The Partin tables, combining preoperative PSA, biopsy Gleason score (GS), and clinical stage, are the most widely used tools to predict final histopathology for organ-confined tumors.[29] The tables were validated in patients admitted at the Mayo Clinic[30] and in European patients.[31] The tables can provide useful information to select those cancers where a safe nerve-sparing procedure can be proposed.

The 7-year biochemical progression-free survival for localized disease was reported to be 79% with RP, 77% with radiation, and 74% with brachytherapy.[32] The prognosis of stage T2 prostate cancer is excellent after RP and this treatment is therefore considered the gold standard, especially when it concerns a high-grade cancer confined to the prostate on pathological examination.[28] Active monitoring is mostly not advisable for low-grade T2 tumors, because the preoperative assessment of tumor grade by needle biopsy is frequently unreliable.[33] Many attempts have been made to predict potential insignificant cancers for which RP might be obvious overtreatment. Combinations of biopsy Gleason score <7, the number and extent of prostate puncture biopsy core invasion <15%,[34] the PSA density <0.10,[35] and the free/total PSA >0.15[20] have all been used to predict insignificant tumors in clinical T1c and T2 cancer. Active monitoring for these tumors, however, remains a difficult exercise. On one hand, the initially detected tumor with a favorable Gleason grade will not continue to be as well differentiated in the following years. Most tumors will dedifferentiate with time, and therefore the effective tumor doubling time cannot be reliably anticipated. This will necessitate repeat biopsies and repeated counseling with patients who will need motivation to further continue on a non-treatment policy. On the other hand, the patient will get older, and while he might have been a candidate for a curative treatment by surgery or radiotherapy in younger years, he will not be considered a candidate for a curative treatment any longer from a certain age where then (palliative) hormonal treatment will remain the only treatment option. Therefore, active monitoring policies need to be further studied; a global prospective randomized trial is planned.[36]

Locally advanced disease

T3a prostate cancer is extracapsular extension (ECE) either unilateral or bilateral and T3b is invasion of seminal vesicles.[10] It is estimated that 12–25% of newly detected prostate cancers are stage T3.[37] Although, since the advent of PSA, the number of patients initially presenting with metastatic disease has dramatically decreased and those with organ-confined disease have increased, the number of patients detected with extracapsular extension remains about the same.

Some years ago, T3 tumors were considered to be advanced disease for which RP was not appropriate and radiation therapy (RT) or androgen deprivation therapy (ADT) were commonly used. Indeed, many urologists were reluctant to perform surgery for clinical T3, because they realized that in a substantial number of patients occult metastatic spread was present, either systemically or in the lymph nodes. Moreover, surgeons were faced with positive surgical margins for which adjuvant treatment measures, e.g. radiotherapy, were then necessary.

At a time when it is important to recognize T3 before treatment, one has tried to improve the diagnostic accuracy of the digital rectal examination (DRE), which, although it has a low positive predictive value, remains the examination of choice. Ultrasound can sometimes be helpful in recognizing extracapsular extension or seminal vesicle invasion. Magnetic resonance imaging (MRI) is also helpful in recognizing seminal vesicle invasion and a contrast-enhanced computed tomography (CT) scan will help in recognizing enlarged nodes. The combination of DRE and transrectal ultrasonography (TRUS) was recently reported to have a 71% sensitivity, 41% specificity, 50% positive predictive value, and 63% negative predictive value.[38]

Some clinicians found that power Doppler ultrasound could improve the accuracy of detection of extracapsular involvement by the presence of vessels perforating the capsule.[39] Others, however, found no advantage in the use of Doppler imaging above gray-scale technique in the detection of clinical unilateral T3a prostate cancer (43.8% vs 49.6%).[38] Nevertheless, overstaging is rather frequent and occurs in an estimated 13–27% of cT3 prostate cancer,[40] the explanation being that an experienced urologist will anticipate pathological capsular perforation and therefore clinically stages a lumpy T2 tumor as a T3 cancer.

Many pretreatment tables and postoperative nomograms predicting histopathology and survival are available in the literature for clinically organ-confined disease, using the combination of preoperative serum PSA, biopsy GS, and clinical stage. Joniau et al elaborated a pretreatment table for clinical T3a cancer and clearly defined six separate risk groups (Table 3.1). This will help the urologist to make an optimal decision for treating cT3 prostate cancer and to preoperatively counsel the patient about eventual adjuvant treatment measures, as in the case of margin positivity, nodal invasion, PSA persistence, or seminal vesicle invasion.[41]

The indications for radiotherapy for cT3-4 prostate cancer resulted from the publication of large randomized trials where radiotherapy alone was compared to radiotherapy with neoadjuvant or adjuvant hormonal treatment.[42,43] These trials described the superiority of the combination treatment but they never showed the superiority of this combination above surgery, either in monotherapy or in combination. In an attempt to obtain a European consensus about the management of cT3 prostate cancer, the authors had to conclude that there was no consensus as to the standard of care and that there were national differences in the proposed treatment strategies.[44] At the same time, it was reported that patients with clinical T3 prostate cancer and well- or moderately well-differentiated tumors benefit from RP while radiotherapy might be more effective in more advanced disease.[45] A single-center RP monotherapy series confirmed that acceptable results could be obtained as long as the T3 cancer was not poorly differentiated.[46] A multi-institutional pooled analysis showed excellent cancer-specific survival rates as long as the tumors were well- or moderately well-differentiated.[47] Another single-center RP monotherapy series, however, showed that the Gleason score (from the biopsy) was not a discriminative factor but, that with low or intermediate PSA levels, excellent biochemical progression-free survival rates could be achieved (60% for PSA <10 and 40% for PSA = 10–25).[48] In this study, the analysis of subgroups following the former TNM classification showed that patients that were pathologically T2 and T3a (unilateral ECE) were doing very well. The poorest outcome was for the pT4 and the pT3b (bilateral ECE), while the pT3c (seminal vesicle invasion) category also achieved reasonable PSA-free survival rates.[48]

Not all patients that undergo surgery for cT3 prostate cancer will be cured by surgery alone.

Table 3.1 Predicted histopathological outcome after radical prostatectomy

Biopsy GS	*Histopathological results*	*PSA ≤10*	*PSA >10–20*	*PSA >20*
≤7 (3 + 4)	Organ-confined pT2	29 (20–39)	21 (12–33)	14 (5–27)
	Extraprostatic extension pT3a	65 (55–74)	63 (49–76)	46 (30–62)
	+ Seminal vesicle pT3b	5 (2–10)	14 (5–24)	32 (18–48)
	+ Adjacent structure pT4	1 (0–2)	2 (0–8)	8 (0–16)
≥7 (4 + 3)	Organ-confined pT2	31 (15–46)	20 (7–36)	9 (2–21)
	Extraprostatic extension pT3a	54 (37–71)	47 (30–65)	23 (9–43)
	+ Seminal vesicle pT3b	12 (4–25)	26 (12–46)	44 (19–69)
	+ Adjacent structure pT4	3 (0–10)	7 (0–17)	24 (0–55)

Certainly, those that proved to be pT2 and those with limited pT3a with just a limited extracapsular extension will be cured but many patients with more advanced cT3 will eventually need adjuvant or salvage radiotherapy or androgen deprivation therapy. However, it has become more and more obvious that surgery has an important role as initial treatment for locally advanced T3 prostate cancer (Table 3.2).[46–52] In summary, these reports showed 5- and 10-year overall survival rates of 75–97.6% and 60–94.8%, respectively. The 5- and 10-year cancer-specific survival was as high as 85–100% and 57–90%, respectively.

In the recent literature, surgery for locally advanced patients was further studied showing that 3 years after surgery the PSA-free survival was 70%.[53] A publication of the SEER data in the period 1995–2001 on 1093 cT4 patients showed an increased survival by surgery compared with radiotherapy alone or hormone therapy. Survival data were comparable to those who were treated with radiotherapy and hormones but the highest survival rates were

Table 3.2 Literature review on the outcome of surgery for clinical locally advanced T3 prostate cancer in different studies

Survival rate	*BPFS*			*CPFS*			*CSS*			*OS*		
Years follow-up (FU) *Authors*	*5*	*10*	*15*	*5*	*10*	*15*	*5*	*10*	*15*	*5*	*10*	*15*
Yamada et al[49] (median FU = 5.4 years) (n = 57)	45.5 (PSA >0.4)			81.4						91.2 (77.6 at 7.5 years)		
Gerber et al[47] (mean FU = 39 months; median FU = 26 months) (n = 242)				72 (meta free)	32		85	57				
Van den Ouden et al[46] (median FU = 52 months) (n = 83)	29 (PSA >0.1)			59	31		85	72		75	60	
Martinez de la Riva et al[50] (mean FU = 68.7 months) (cT3a only) (n = 83)	59.8 (PSA >0.3)						100			97.6	94.8	
Ward et al[51] (median FU = 10.3 years) (n = 841)	58 (PSA >0.4)	43	38	85	73	67	95	90	79	90	76	53
Hsu et al[52] (mean FU = 70.6 months) (unilateral cT3a only) (n = 200)	59.5 (PSA >0.2)	51.1		95.9	85.4		98.7	91.6		95.9	77	

BPFS = biochemical progression-free survival; CPFS = clinical progression-free survival; CSS = cancer-specific survival; OS = overall survival.

obtained in the RP group.[54] Seminal vesicle invasion was by many considered as systemic disease but, as shown by Van Poppel et al in 2000,[48] these patients also have a chance of cure with surgery alone. A recent prospective study on 387 patients with pathological invasion of the seminal vesicles confirmed that seminal vesicle invasion does not impact on PSA recurrence after RP and lymph node dissection. At 15 years, 33% of pT3bN0 patients remained PSA relapse free.[55] The surgical technique of a RP for locally advanced T3 cancer is different from that applied in locally confined tumors. The surgery includes an extensive lymph node dissection, a broad neurovascular bundle resection at least at the tumor-bearing side, a complete resection of the seminal vesicles, and, in many cases, the resection of the bladder neck.[40–56]

Neoadjuvant hormonal treatment

The application of hormonal manipulation before RP has been quite extensively investigated in a number of studies that have, however, mainly focused on cT2 and much less on cT3 prostate.[57–63] Most studies gave 3 months of luteinizing hormone-releasing hormone (LHRH) (with or without antiandrogen); one study gave 6 weeks of estramustine phosphate (Estracyt);[59] another study gave 3 months of cyproterone acetate before surgery.[62] The table summarizing these reports shows that only a few patients with locally advanced prostate cancer were included. Unfortunately, none of these studies was powered to have overall or cancer-specific survival as an endpoint (Table 3.3).

They clearly showed that in the cT2 cancers, the number of positive margins was dramatically decreased (with the well-known difficulties in interpretation of margin positivity by the pathologist after hormonal manipulation). Nevertheless, the biochemical progression and clinical progression were identical in both arms. Therefore, some authors have tried to prolong treatment in order to further decrease the occurrence of positive margins in cT2.[64–66] By giving hormonal treatment for more than 4 months,

Table 3.3 Reported randomized trials on neoadjuvant hormonal treatment before radical prostatectomy in T2 and T3 prostate cancer

Author	*No. of cases/stage*	*Treatment/follow-up (FU)*
Labrie et al[57]	134 T2, 27 T3	3 months LH + AA FU ?
Witjes et al[58]	220 T2, 182 T3	3 months LH + AA FU = 4 years
Van Poppel et al[60]	84 T2, 68 T3	6 weeks Estracyt FU = 4 years
Soloway et al[61]	282 T2b	3 months LH + AA FU = 4 years
Klotz et al[62]	213 T2	3 months CPA FU = 6 years
Aus et al[63]	45 T1T2a, 81 T2b-T3a	3 months LHRH FU = 7 years

LH, luteinizing hormone; AA, antiandrogen; CPA, cyproterone acetate; LHRH, luteinizing hormone-releasing hormone.

up to 8 months or even up to 22 months before surgery, the positive margin rate was decreased to, respectively, 6.4% and 2%. But again, in a randomized study of 3 vs 8 months of androgen blockade, there was no difference shown in biochemical progression.[67] Therefore, the use of neoadjuvant treatment in clinically locally confined prostate cancer has been abandoned. The value of this treatment strategy in cT3 is unknown; there might be an advantage for high-risk patients, with a high PSA or with poorly differentiated tumors, but no study has been designed to demonstrate this. Nevertheless, there has been a T3–T4 Phase II study by the SWOG (South Western Oncology Group) trial 91.09. It was a prospective non-randomized trial including mostly T3 (97%), but also some T4 cases (3%) with large tumors (39% were >4 cm in diameter). The PSA varied between 2.6 and 407.0 (mean = 19.8 ng/ml). The Gleason score was 7 or higher in 67% of patients (25% were Gleason 8, 9, or 10). They were all N0M0 on CT scan and bone scan and had neoadjuvant LHRH and an antiandrogen for 4 months. The mean follow-up was 6.1 years (4.6–7 years). As expected, there was a significant tumor volume reduction in 98% of patients and the PSA became undetectable in 55% of patients. The pathological stage was pT3b in 31, pN1 in 19, and the margin positive rate was 30%. But, importantly, 70% of the patients were biochemically without evidence of disease at 5 years and the overall survival at 5 years was 90%.[68] These results for locally advanced tumors are better than those that can be obtained with a combination of hormones and radiotherapy. The question remains whether these better results are obtained because of the neoadjuvant hormonal treatment. Since to date we have no results on neoadjuvant treatment in cT3 concerning overall survival, one cannot conclude that neoadjuvant treatment in this patient category is completely obsolete. The jury is still out: it might be that a subgroup could benefit but there is no properly designed randomized study to show it.[69]

Salvage/adjuvant radiation or hormonal treatment

In 2005 a very important report from the Mayo Clinic was published in which the value of adjuvant or salvage hormone therapy and radiotherapy was analyzed. Of a total of 841 RPs for cT3 prostate cancer 51% of patients had adjuvant hormone treatment immediately after surgery, 26% had salvage hormone therapy for biochemical or clinical relapse later during the disease evolution. Adjuvant radiotherapy immediately after RP was given in 16% of patients, while 15% had salvage radiotherapy later. In this paper the authors showed that by a multimodal therapy comprising surgery as a first step and sometimes followed by immediate or delayed hormonal or radiation treatment, clinical progression-free survival and cancer-specific survival rates at 15 years could be obtained that are comparable to those in cT2 prostate cancer.[51] More recently, the EORTC (European Organization for Research and Treatment of Cancer) published results of postoperative radiotherapy after RP. EORTC trial 22911 showed an improved biochemical progression-free survival achieved by the combination treatment that was statistically significantly better than in those patients who had no further treatment ($p < 0.0001$). This biochemical progression-free survival was seen in the different risk groups and was seen in all patient categories that were included, i.e. the pT2 patients with positive margins, the pT3 patients with negative margins, the pT3 patients with positive margins, and those with seminal vesicle invasion.[70] In a forest plot, however, it was obvious that patients with pT3 and negative margins benefited only marginally from postoperative radiation treatment.[71]

This study has shown that delivering postoperative radiotherapy in these patients improves biochemical progression-free survival when compared with patients who do not have postoperative radiation treatment, and sometimes never receive salvage radiotherapy or hormonal manipulation. It is not certain whether patients with an undetectable PSA in these pathological stages of the disease warrant immediate postoperative radiotherapy or can be delayed adjuvant treatment until a twice-confirmed minute PSA relapse occurs later in the postoperative course. No tumor in the human being has a tumor marker like PSA, which, certainly after RP, allows a very strict follow-up and can indicate salvage treatment that depends on the time of PSA recurrence and its velocity. In a well-described cohort of 281 participants of a population-based randomized screening trial who underwent radical prostatectomy, the majority of men with positive margins did not experience PSA relapse even in the absence of adjuvant radiotherapy.[72] In the randomized EORTC study, however, when positive margins were obtained during RP for locally advanced prostate cancer, radiation treatment was shown to be efficient in prolonging biochemical progression-free survival. In this trial there was no difference between positive margins at the apex or posterolateral positive margins. Therefore, it might be reasonable to propose postoperative radiation treatment in the case of an obvious positive margin. In patients with dubious or focal positive margins, again, a PSA follow-up and eventual salvage radiotherapy in a delayed fashion can be defended.

We recently reviewed our own experience with RP in cT3 prostate cancer patients that underwent surgical treatment.[52] Of 200 patients included, 23.5% were pT2, 56.5% were pT3a, 16% pT3b, and 4.4% pT4; 8.5% had positive nodes (1 or 2 nodes invaded), 33.5% had positive surgical margins, and 56% of them received adjuvant or salvage therapy. The 5-year and 10-year biochemical progression-free survival was approximately 60% and 50%, respectively, but the cancer-specific survival was as high as 99% and 92%, while the overall survival was 96% and 77%, meaning that a treatment for cT3 prostate cancer starting with surgery gives excellent cancer-specific survival rates despite the locally advanced stage. In a multivariate Cox regression analysis, the surgical margin was the only statistically significant factor determining biochemical progression-free survival ($p < 0.00001$). This means that the surgeons need to be trained in order to be able to obtain negative surgical margins in these locally advanced stages. The pathological stage and the cancer volume were not statistically significant factors in multivariate analysis.[52]

In conclusion, clinical T3 prostate cancer is a disease that will often warrant multimodal treatment. Starting with surgery is giving a chance for cure not only in the pT2 but also in some pT3 patients just with RP alone. The definitive pathology of the resected specimen can show risk factors like seminal vesicle invasion or microscopic nodal invasion that can indicate immediate hormone treatment when the PSA has not become undetectable after surgery. Obvious positive surgical margins can be treated with immediate radiotherapy even when the PSA is undetectable. Serum PSA allows a follow-up that will indicate appropriate salvage and adjuvant measures whenever needed. Hormone therapy in combination with radiotherapy should not any longer be considered as the treatment of choice for cT3 prostate cancer.

PATIENT-RELATED INDICATIONS

Age

Prostate cancer can be found in young patients, even younger than 30 years old.[73] The age-specific relative survival rate does not differ significantly among different age groups, although some authors have suggested that younger patients should be given more aggressive treatment than older patients.[74] In the analysis of data from 6514 patients with prostate cancer, they found that 85% of these patients died during 7–23 years of follow-up, and that 55%

died of prostate cancer. The patients diagnosed before the age of 60 had an 80% risk of dying of prostate cancer, whereas patients over 80 had less than 50% risk. They concluded prostate cancer mortality is high but decreased in older patients, so that age at diagnosis was found to be a strong predictor of prostate cancer death.[75] Others reported that patients over 65 years were more likely to experience distant failure than younger patients and age greater than 65 years was a significant independent predictor of distant metastases.[76] Age is considered a strong predictor of the probability of curable cancer, and early detection efforts in younger men are likely to decrease the prostate cancer mortality.[77] Young men who are candidates for radical prostatectomy have potentially curable disease, particularly if PSA at the time of diagnosis is <10 ng/ml.[78] From a study of 2897 men with localized prostate cancer who underwent RP, it was shown that patients with age <50 years had a better long-term cancer control.[79] Also, another group reported on 477 men with RP, where younger patients (<50 years old) had a better disease-free survival probability.[80] Another study on 489 patients with RP for localized prostate cancer found biochemical recurrence in 12% of patients <70 years and in 25% >70 years.[81] However, in a recent study there was no significant difference in survival between the patients aged less than or more than 71 years old.[82]

In conclusion, RP can be performed in motivated healthy older patients, but a careful selection regarding comorbidities and possible complications such as urinary incontinence is warranted. Younger age is certainly not an unfavorable factor and early detection of prostate cancer and early treatment of significant cancer therefore remains the only acceptable management strategy.

Body mass index

Obesity is a common problem in the Western world. Increasing body mass index (BMI) is associated with increasing odds of capsular incision during radical prostatectomy, which can result in margin positive disease despite the tumor being locally confined. Mild obesity was associated with 30% increasing odds of capsular incision, whereas moderate and severe obesity were associated with 57% increasing odds of capsular incision compared with normal-weight patients.[83] Not only is the technique of retropubic RP more difficult in obese patients but also increasing BMI was associated with higher-grade disease in the RP specimen, more positive surgical margins, more frequent extraprostatic extension, and lymph node involvement and subsequently an increasing risk of biochemical progression.[84] Since obesity can influence the outcome after RP, surgeons should be careful to select obese patients and to counsel them about the risk of their physical condition.

EUROPEAN AND AMERICAN GUIDELINES

Following the *AUA guidelin*es, published in 1995, RP is recommended in patients with T1 or T2 tumors after careful assessment of the life expectancy, overall health status, and tumor characteristics. Life expectancy, rather than patient age, has to be considered in treatment selection. The expected longevity should be longer than the expected morbidity of the patient's cancer if left untreated. To evaluate the surgical risk factors, the Charlson score and ECOG (Eastern Cooperative Oncology Group) performance status may be useful to assess the overall health status, which will influence life expectancy. Small, well-differentiated cancers progress more slowly and are less likely to be life threatening than large, poorly differentiated tumors, which have a greater potential to be biologically aggressive and clinically significant.[85]

According to the *EAU guidelines*, RP for T1a prostate cancer is an option in younger patients with a long life expectancy, especially for poorly differentiated tumors. In patients with well or moderately differentiated tumors and life expectancy <10 years, the standard treatment is watchful waiting. In patients with a life expectancy >10 years, restaging by TRUS and biopsy is advised. For T1b to T2 disease, RP is standard treatment for patients with a life expectancy >10 years who accept the treatment-related complications. For locally advanced disease, RP is an option for selected patients with rather limited T3a and Gleason score 5–7 on biopsy, with a rather low PSA and a life expectancy of >10 years. The guidelines do not specify the cut-off for volume and for preoperative PSA level.[86]

The guidelines on the management of prostate cancer by the Royal College of Radiologists and the British Association of Urological Surgeons mention that localized T1-T2 and N0 and M0 can be treated by surveillance, except for patients with poorly differentiated tumors. RP may be more appropriate than surveillance for some patients with poorly differentiated tumors. In patients with an estimated life expectancy of more than 10 years, if the age is more than 60 years old, RP, RT, or surveillance may be considered. If the age is less than 60 years old, RP can be considered but the patient should be counseled about the risk of impotence and incontinence. In patients with locally advanced T3-4, N0, M0 disease, the guidelines suggest RT, with or without neoadjuvant or adjuvant ADT, ADT alone, or 'watch and wait'. Radical prostatectomy is not recommended to treat this stage of disease.[87]

The National Cancer Institute (NCI) suggests that surgery should be reserved for patients in good health who are younger than 70 years old and who want surgical intervention. The patients should have a negative bone scan and tumors confined to the prostate gland (stage I and stage II). In stage III, RP and pelvic lymphadenectomy may be performed in highly selected patients. The guidelines did not detail the criteria to select cT3 prostate cancer candidates for radical prostatectomy.[88]

The clinical practice guidelines in oncology for prostate cancer by the National Comprehensive Cancer Network (NCCN) suggest that RP is an appropriate treatment for clinically localized prostate cancer that can be completely excised surgically in patients who have a life expectancy of 10 years or more and no serious comorbid conditions that would contraindicate an elective operation. The guidelines also mention that radical prostatectomy and pelvic lymph node dissection is appropriate in selected patients with T3 or N+ cancer within the context of an eventual multimodal treatment plan.[89]

In conclusion, most guidelines agree that radical prostatectomy is the gold standard for localized prostate cancer. For locally advanced disease, conservative treatments can also be recommended, including RT, ADT, or a combination. We consider cT3 a surgical disease in well-selected patients in the frame of a multimodal treatment strategy.

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CHAPTER 4

Clinical predictors of organ-confined prostate cancer

Danil V Makarov and Alan W Partin

INTRODUCTION

Radical prostatectomy (RP) offers the best chance for the cure of prostate cancer (CaP) when disease is localized.[1,2] Accurate prediction of pathological stage is fundamental to determining which patients will derive the most benefit from RP.[3] Many preoperative variables exist which may be used to predict postoperative stage and suggest a localized or a systemic treatment approach. The most commonly used variables are digital rectal examination (DRE), prostate-specific antigen (PSA), and prostate biopsy Gleason score.

Whereas each of these factors is predictive by itself, a better prediction can be made using a combination of these factors. To this end, our group, along with others, have previously published nomograms to predict the presence of organ-confined CaP.[4–12] Our approach combines the three most commonly available preoperative variables (tests) – serum PSA, clinical (TNM) stage, and biopsy Gleason score – into a model, the 'Partin tables', using data from a large series of patients to provide the likelihood of various final pathological stages at RP.[4–6]

PROSTATE-SPECIFIC ANTIGEN

PSA is recognized as the most useful biomarker for the diagnosis, staging, and monitoring of prostate cancer today.[13] By itself, PSA has been demonstrated to be associated with advancing clinical and pathological stage.[14–16] Ercole et al[14] performed an early retrospective study including 209 men with various stages of CaP: 59% of men with extracapsular disease had PSA levels >10 ng/ml compared with only 7% of men with organ-confined disease. Conversely, 93% of men with PSA >10 ng/ml had extracapsular disease.

Catalona et al[17] used serum PSA to screen 1653 self-referred volunteers >50 years old and then biopsied those men with PSA >4.0 ng/ml. The results were compared with those of 300 consecutively studied men ≥50 years old who underwent ultrasound-directed biopsy because of symptoms or abnormal findings on rectal examination: 6.5% of these men had PSA between 4.0 and 9.9 ng/ml, and 22% of those had prostate cancer on biopsy; 1.8% of the men had PSA >10.0 ng/ml, and 67% of those men had prostate cancer. Serum PSA measurement had the lowest error rate of any of the available diagnostic modalities.

However, despite the repeated demonstration of the association between PSA and tumor stage, the substantial overlap of PSA among the various stages makes PSA less useful as a solo screening method.[18] Whereas tumor volume influences PSA in many studies, other factors influence PSA as well.[19] Indeed, while elevated PSA is commonly thought of as a marker for more advanced prostate cancer, Partin et al[16] have demonstrated that advanced-stage, high-grade, larger tumors may produce less PSA than their less aggressive counterparts. It is not possible with current biomarkers to distinguish the contributions that benign prostatic hyperplasia (BPH) and CaP make to an individual's PSA without examining a surgical specimen.

When considering PSA for staging of prostate cancer, it is important to note the changes in the predictive ability of this test that have occurred over time. Stage migration has led some groups to doubt whether any association at all remains between PSA and CaP. Indeed, Stamey et al,[20] in a very controversial 2004 study, suggested that the PSA era might be over. In their study, the authors observed that over time at presentation, tumor stage, mean patient age, mean tumor size, and mean PSA have become lower. They also noted that while, in the past, PSA was associated with tumor volume on pathological specimens, in recent years, the only pathological variable with which it was associated was prostate size. Freedland et al[21] came out with a rebuttal, stating that, while PSA may not be associated with tumor size in men undergoing radical retropubic prostatectomy (RP), an elevated PSA is still associated with higher-grade cancer, more adverse pathological features, and the risk of biochemical progression on multivariable analysis. They conclude that, after all, the PSA era is alive and well.

GLEASON SCORE

Of the many histological grading systems introduced to help predict pathological stage and prognosis for prostate cancer, the most commonly used is the Gleason system for tumor grading. The general trend observed among surgical cases at Johns Hopkins Hospital has been that higher Gleason biopsy grades are associated with worsening pathological stage. However, this observation is not always true on an individual basis.[18]

The Gleason score is based on a low-power microscopic description of the histological architecture of the cancer.[22] The specifics of Gleason grade determination are discussed in Chapter 3 and are beyond the scope of this chapter. However, simply, a Gleason score between 2 and 10 is assessed by adding the primary pattern visible in the sample to the secondary pattern.

A Gleason score of 7 or greater on preoperative needle biopsy is correlated with worse pathology and prognosis than a Gleason score of 6 or less. In 955 men who had undergone RP for clinically localized disease, Partin et al[23] determined that there existed marked differences in actuarial recurrence-free probabilities for men with tumors of Gleason score < 7 compared with those with tumors of Gleason score ≥ 7 when there is pathologically established capsular penetration. Also, the presence of any Gleason pattern 4 has been determined to be predictive of postoperative biochemical failure.[24] Interestingly, the relative amount of Gleason pattern 4 on needle biopsy has been shown to be important in the staging of prostate cancer. Makarov et al[25] determined that Gleason score $4 + 3$ on needle biopsy was associated with worse pathological outcomes, independent of the number of cores involved with cancer (a marker for tumor volume).

The Gleason grade is an excellent predictor of pathological stage, but, similar to PSA, it suffers from significant limitations when used in isolation. The preoperative Gleason score determined from biopsy specimens has been shown to correlate closely with the final pathological stage for patients at either extreme of the system (i.e. 2–4 and 8–10).[16] Unfortunately, most men present with Gleason scores of 5–7, where biopsy Gleason score does not predict pathological stage as accurately.[26]

DIGITAL RECTAL EXAMINATION

Digital rectal examination is the oldest and simplest test for prostate cancer, and is specifically used to evaluate the cancer's local extent.[18] DRE has only fair reproducibility in experienced hands. Smith and Catalona[27] undertook a study wherein DRE was performed in 116 volunteers by different urologists, each blinded to the other's interpretation, performing the examinations. Examiners independently agreed on DRE findings being either normal or suspicious for cancer in 84% of subjects. However, adjusting for chance agreement, the agreement between examiners was only fair.

DRE can miss a substantial number of significant cancers, and often detects only those which are too far advanced to be amenable to localized treatment.[26] In a previously discussed study by Catalona et al[17] from 1991, the group estimated that if rectal examination alone had been used to screen men receiving biopsies, 32% of cancers suggested by an elevated serum PSA would have been missed.

In the first paper describing the Partin tables in 1993, Partin et al[4] described the performance characteristics of DRE. In a group of 591 men who had undergone RRP at Johns Hopkins Hospital, 565 men had normal DREs and 36 men had DREs suspicious for CaP. Of the men with normal DRE, only 52% had organ-confined disease on pathology, whereas in men with abnormal DREs, 89% had disease outside of the prostate. Thus, in a population of men undergoing radical prostatectomy for biopsy-proven prostate cancer, DRE by itself only has sensitivity of 53% and a specificity of 81% for the prediction of organ-confined disease.

THE PARTIN TABLES

Original

Partin et al[4] recognized in 1993 that although PSA, Gleason grade, and DRE were independently fair predictors of localized CaP, the combination of these factors might yield a superior predictive capability than any one alone. The authors used logistic regression analysis to assess the utility of combining these variables as predictors of final pathological stage. Their original cohort included 703 men who had undergone radical prostatectomy for clinically localized prostate cancer. They demonstrated that the combination of all three variables more accurately predicted final pathological stage than any single variable alone. From these analyses probability plots and nomograms were constructed to assist urologists in predicting final pathological stage for patients with clinically localized prostate cancer. These became known as 'the Partin tables'.

The data for the original Partin tables proved to be extremely useful for physicians and patients in determining whether they had organ-confined or extraprostatic disease and helping guide their therapy. However, as data to construct these models were collected from men treated between 1982 and 1991, the original model became obsolete, as surgery for CaP and PSA screening for CaP became increasingly widespread. During that time, an ever-increasing percentage (and number) of men have presented with serum PSA levels between 2.5 and 10.0 ng/ml, Gleason scores of 6, normal DREs (clinical stage T1c), and, most importantly, with localized organ-confined disease.

Updates and validations

A multi-institutionally updated version of the Partin tables was performed 4 years later. This nomogram was based on data from men undergoing surgery between 1982 and 1996:[5] 4133 men treated by multiple surgeons across three tertiary care centers specializing in prostate cancer were used to develop the model. This time, bootstrapping was used to estimate the predicted probabilities and confidence intervals for each pathological stage variable, as well as to estimate the modest overall predictive power.

This landmark paper confirmed that the combination of PSA, biopsy Gleason score, and clinical stage (DRE) could be used to predict accurately a patient's pathological stage prior to surgery.

The Partin tables have been validated in various clinical settings ranging from academic medical centers in the United States,[28] Canada,[29] and Turkey[30] to cohorts of patients in a community setting.[31] A further update to account for continuing stage migration was made in 2001, examining patients treated at Johns Hopkins Hospital from 1994 to 2000.[6]

The 2007 Partin tables

The American Cancer Society reported this year a continued decrease in CaP death rates, with an estimate that 90% of patients newly diagnosed this year will present with either local or regional disease.[32] This trend or stage migration, whether the result of improved early detection CaP or a change in the biology of, has resulted in a dramatic shift in the stage at presentation for men with newly diagnosed disease.[33]

Therefore, previously determined staging algorithms less accurately reflect the status of the contemporary cohort of men presenting with CaP. To address this problem, Makarov et al[34] have updated the Partin tables with a more contemporary cohort of men treated since 2000 at Johns Hopkins Hospital with revised Gleason and clinical stage. These predictions are presented within Tables 4.1, 4.2 and 4.3.

Between 2000 and 2005, 5734 men with clinically localized CaP who received no neoadjuvant hormonal or radiation therapy underwent RP and a staging pelvic lymphadenectomy at the Johns Hopkins Hospital. All men enrolled in this cohort had a preoperative serum PSA, a biopsy Gleason score determined at our institution, and a clinical stage assigned by the attending physician (AJCC-TNM, 1992/2002) of T1c, T2 (a, b, or c). Exclusion criteria included missing preoperative information, neoadjuvant hormonal therapy, preoperative treatment with 5α-reductase inhibitors, chemotherapy, or hormonally active herbal therapies.

Statistical analysis

Multivariable logistic regression analysis was performed to develop a predictive model for the non-ordered pathology outcome categories: organ-confined, extraprostatic extension, seminal vesicle involvement, or lymph node metastasis. PSA levels before surgery were categorically divided into 0–2.5, 2.6–4.0, 4.1–6.0, 6.1–10, and >10.0 ng/ml, TNM clinical stage was examined (AJCC-TNM, 1992/2002) as T1c, T2a, and the combination of T2b and T2c. Biopsy Gleason score sum was divided categorically as 5–6, 3 + 4 = 7, 4 + 3 = 7, and 8–10. In contrast to prior versions of the Partin tables, men with Gleason sum less than 5 were excluded from analysis.

In this cohort, 5734 men, average age 57.4 ± 6.4 years (range 34–75), who met the enrollment criteria, were consecutively enrolled (Table 4.1). Eighty-nine percent of the men were Caucasian and 6% African-American. The final pathological stage demonstrated that 73%, 22%, 3%, and 1% had organ-confined disease, extraprostatic extension, seminal vesicle involvement, or lymph node involvement, respectively.

We combined clinical stages T2b and T2c, and combined PSA categories 6.1–8.0 with 8.1–10.0, to create a better-fitting model. We stratified Gleason score into modified groups based on the risk of recurrence. Previous work from Johns Hopkins Hospital demonstrated Kaplan–Meier actuarial survival curves (data not shown) for men with follow-up of more than 8 years showing biochemical progression-free survival was similar between tumors with Gleason score of 5 or 6. The same held true for tumors with Gleason score 8–10.[35] Thus, these Gleason scores were grouped as 5–6 or 8–10. Biopsy Gleason scores below 5 were excluded.[36] Previous data have also demonstrated that Gleason sums of 3 + 4 = 7 and 4 + 3 = 7 behave differently and warrant substratification.[37]

Text continued on page 49

Table 4.1 Demographics of men undergoing radical prostatectomy

Characteristic	*No.*	*(%)*
No. of patients	5730	
Mean age +/–SD	57.4 +/–6.4	
No. Race (%)		
Caucasian	5081	(89)
African-American	372	(7)
Hispanic	56	(1)
Asian	58	(1)
Other	158	(3)
PSA groups (ng/ml)		
0 to 2.5	452	(8)
2.6 to 4.0	946	(17)
4.1 to 6.0	1994	(35)
6.1 to 8.0	1093	(19)
8.1 to 10.0	578	(10)
> 10.0	667	(12)
Biopsy Gleason score, No (%)		
5–6	4402	(77)
3 + 4 = 7	816	(14)
4 + 3 = 7	348	(6)
≥8	164	(3)
Clinical stage (AJCC-TNM 2002)		
T1c	4419	(77)
T2a	998	(17)
T2b	279	(5)
T2c	34	(1)
Prostatectomy Gleason score, No. (%)		
5–6	3693	(64)
3 + 4	1304	(23)
4 + 3	425	(7)
8–10	308	(5)
Organ confined	4204	(73)
Extraprostatic extension (SV-, LN-)	1276	(22)
Seminal vesicle involvement (LN-)	180	(3)
Lymph node involvement	70	(1)

Table 4.2 Demographic information of men included in previous versions of the Partin tables

Year of publication	*1993*		*1997*		*2001*		*2007*	
Characteristic	*No.*	*(%)*	*No.*	*(%)*	*No.*	*(%)*	*No.*	*(%)*
Years of treatment	*1982 to 1991*		*1982 to 1996*		*1994 to 2000*		*2000 to 2005*	
No. of patients	703		4133		5079		5730	
Mean age +/– SD					57.9 +/– 6		57.4 +/– 6.4	
No. Race (%)								
Caucasian					4571	(90)	5081	(89)
African-American					305	(6)	372	(7)
Hispanic							56	(1)
Asian							58	(1)
Other							158	(3)
PSA groups (ng/ml)								
0 to 2.5	†		†		356	(7)	452	(8)
2.6 to 4.0	284	(40)	943	(23)	508	(10)	946	(17)
4.1 to 6.0	*		*		1371	(27)	1994	(35)
6.1 to 10.0	246	(35)	2006	(48)	1778	(35)	1671	(29)
>10.0	173	(25)	1184	(29)	1067	(21)	667	(12)
Biopsy Gleason score, No (%)								
2–4	64	(9)	222	(5)	30	(0.6)	‡	
5–6	471	(67)	2783	(67)	4012	(79)	4402	(77)
3 + 4 = 7	**		**		660	(13)	816	(14)
4 + 3 = 7	130	(19)	906	(22)	223	(4.4)	348	(6)
≥8	38	(5)	222	(5)	152	(3)	164	(3)

Clinical Stage (AJCC-TNM 1992/2002)								
T1a	31	(4)	74	(1)	‡		‡	
T1b	71	(10)	149	(3)	‡		‡	
T1c	n/a		1358	(33)	3250	(64)	4419	(77)
T2a	326	(46)	1186	(29)	1524	(30)	998	(17)
T2b	179	(26)	852	(21)	203	(4)	279	(5)
T2c	60	(9)	398	(10)	102	(2)	34	(1)
T3a	36	(5)	116	(3)	‡		‡	
Pathologic stage								
Organ confined	382	(54)	1957	(48)	3251	(64)	4204	(73)
Extraprostatic extension (SV-, LN-)	203	(29)	1661	(40)	1524	(30)	1276	(22)
Seminal vesicle involvement (LN-)	44	(6)	303	(7)	203	(4)	180	(3)
Lymph node involvement	74	(11)	212	(5)	1016	(2)	70	(1)

†: 0–4 combined
*: 4–10 combined
‡: excluded from analysis
**: all 7s combined
n/a: not applicable

Table 4.3 Nomograms predicting pathologic stage of CaP based on clinical stage (TNM), PSA, and Gleason score

Clinical stage T1c (nonpalpable, PSA elevated) N = 4419					
		Biopsy Gleason score			
PSA range (ng/ml)	*Pathologic stage*	***5–6***	***3 + 4 = 7***	***4 + 3 = 7***	***8–10***
0–2.5	Organ confined (*N* = 226)	**93 (91–95)**	**82 (76–87)**	**73 (64–80)**	**77 (65–85)**
	Extraprostatic extension (*N* = 19)	**6 (5–8)**	**14 (10–18)**	**20 (14–28)**	**16 (11–24)**
	Seminal vesicle (+) (*N* = 1)	0 (0–1)	2 (0–5)	2 (0–5)	3 (0–8)
	Lymph node (+) (*N* = 3)	0 (0–1)	2 (0–6)	4 (1–12)	3 (1–12)
2.6–4.0	Organ confined (*N* = 619)	**88 (86–90)**	**72 (67–76)**	**61 (54–68)**	**66 (57–74)**
	Extraprostatic extension (*N* = 92)	**11 (10–13)**	**23 (19–27)**	**33 (27–39)**	**26 (19–34)**
	Seminal vesicle (+) (*N* = 8)	1 (0–1)	4 (2–7)	5 (2–8)	7 (3–13)
	Lymph node (+) (*N* = 1)	0 (0–0)	1 (0–1)	1 (0–3)	1 (0–3)
4.1–6.0	Organ confined (*N* = 1266)	**83 (81–85)**	**63 (59–67)**	**51 (45–56)**	**55 (46–64)**
	Extraprostatic extension (*N* = 297)	**16 (14–17)**	**30 (26–33)**	**40 (34–45)**	**32 (25–40)**
	Seminal vesicle (+) (*N* = 37)	1 (1–1)	6 (4–8)	7 (4–10)	10 (6–15)
	Lymph node (+) (*N* = 12)	0 (0–0)	2 (1–3)	3 (1–6)	3 (1–6)
6.1–10.0	Organ confined (*N* = 989)	**81 (79–83)**	**59 (54–64)**	**47 (41–53)**	**51 (41–59)**
	Extraprostatic extension (*N* = 281)	**18 (16–19)**	**32 (27–36)**	**42 (36–47)**	**34 (26–42)**
	Seminal vesicle (+) (*N* = 36)	1 (1–2)	8 (6–11)	8 (5–12)	12 (8–19)
	Lymph node (+) (*N* = 5)	0 (0–0)	1 (1–3)	3 (1–5)	3 (1–5)
>10.0	Organ confined (*N* = 324)	**70 (66–74)**	**42 (37–48)**	**30 (25–36)**	**34 (26–42)**
	Extraprostatic extension (*N* = 165)	**27 (23–30)**	**40 (35–45)**	**48 (40–55)**	**39 (31–48)**
	Seminal vesicle (+) (*N* = 25)	2 (2–3)	12 (8–16)	11 (7–17)	17 (10–25)
	Lymph node (+) (*N* = 13)	1 (0–1)	6 (3–9)	10 (5–17)	9 (4–17)

Clinical stage T2a (palpable < ½ of one lobe) N = 998

PSA range (ng/ml)	*Pathologic stage*	*Biopsy Gleason score*			
		5–6	***3 + 4 = 7***	***4 + 3 = 7***	***8–10***
0–2.5	Organ confined ($N = 156$)	**88 (84–90)**	**70 (63–77)**	**58 (48–67)**	**63 (51–74)**
	Extraprostatic extension ($N = 18$)	**12 (9–15)**	**24 (18–30)**	**32 (24–41)**	**26 (18–36)**
	Seminal vesicle (+) ($N = 2$)	0 (0–1)	2 (0–6)	3 (0–7)	4 (0–10)
	Lymph node (+) ($N = 1$)	0 (0–1)	3 (1–9)	7 (1–17)	6 (1–16)
2.6–4.0	Organ confined ($N = 124$)	**79 (75–82)**	**57 (51–63)**	**45 (38–52)**	**50 (40–59)**
	Extraprostatic extension ($N = 49$)	**20 (17–24)**	**37 (31–42)**	**48 (40–55)**	**40 (30–50)**
	Seminal vesicle (+) ($N = 5$)	1 (0–1)	5 (3–9)	5 (3–10)	8 (4–15)
	Lymph node (+) ($N = 0$)	0 (0–0)	1 (0–2)	2 (0–5)	2 (0–4)
4.1–6.0	Organ confined ($N = 171$)	**71 (67–75)**	**47 (41–52)**	**34 (28–41)**	**39 (31–48)**
	Extraprostatic extension ($N = 101$)	**27 (23–31)**	**44 (39–49)**	**54 (47–60)**	**46 (37–54)**
	Seminal vesicle (+) ($N = 10$)	1 (1–2)	7 (4–10)	7 (4–11)	11 (6–17)
	Lymph node (+) ($N = 3$)	0 (0–1)	2 (1–4)	5 (2–8)	4 (2–9)
6.1–10.0	Organ confined ($N = 142$)	**68 (64–72)**	**43 (38–48)**	**31 (26–37)**	**36 (27–44)**
	Extraprostatic extension ($N = 99$)	**29 (26–33)**	**46 (41–51)**	**56 (49–62)**	**47 (37–56)**
	Seminal vesicle (+) ($N = 12$)	2 (1–3)	9 (6–13)	9 (5–14)	13 (8–20)
	Lymph node (+) ($N = 6$)	0 (0–1)	2 (1–4)	4 (2–8)	4 (1–8)
>10.0	Organ confined ($N = 36$)	**54 (49–60)**	**28 (23–33)**	**18 (14–23)**	**21 (15–28)**
	Extraprostatic extension ($N = 47$)	**41 (35–46)**	**52 (46–59)**	**57 (48–66)**	**49 (39–59)**
	Seminal vesicle (+) ($N = 9$)	3 (2–5)	12 (7–18)	11 (6–17)	17 (9–25)
	Lymph node (+) ($N = 7$)	1 (0–3)	7 (3–14)	13 (6–24)	12 (5–22)

Continued

Table 4.3 Nomograms predicting pathologic stage of CaP based on clinical stage (TNM), PSA, and Gleason score—*cont'd*

Clinical stage T2b (palpable, ≥ ½of lope) or T2c (palpable both lobes) N = 313					
PSA range (ng/ml)	*Pathologic stage*	*Biopsy Gleason score*			
		5–6	***3 + 4 = 7***	***4 + 3 = 7***	***8–10***
0–2.5	Organ confined (*N* = 16)	**84 (78–89)**	**59 (47–70)**	**44 (31–58)**	**49 (32–65)**
	Extraprostatic extension (*N* = 10)	**14 (9–19)**	**24 (16–33)**	**29 (19–42)**	**24 (14–36)**
	Seminal vesicle (+) (*N* = 0)	1 (0–3)	6 (0–14)	6 (0–14)	8 (0–21)
	Lymph node (+) (*N* = 0)	1 (0–3)	10 (2–25)	19 (4–40)	17 (3–42)
2.6–4.0	Organ confined (*N* = 28)	**74 (68–80)**	**47 (39–56)**	**36 (27–45)**	**39 (28–50)**
	Extraprostatic extension (*N* = 15)	**23 (18–29)**	**37 (28–45)**	**46 (36–55)**	**37 (27–48)**
	Seminal vesicle (+) (*N* = 3)	2 (1–5)	13 (7–21)	13 (7–22)	19 (9–32)
	Lymph node (+) (*N* = 2)	0 (0–1)	3 (0–7)	5 (0–14)	4 (0–13)
4.1–6.0	Organ confined (*N* = 46)	**66 (59–72)**	**36 (29–43)**	**25 (19–32)**	**27 (19–37)**
	Extraprostatic extension (*N* = 40)	**30 (24–36)**	**41 (33–47)**	**47 (38–55)**	**38 (28–48)**
	Seminal vesicle (+) (*N* = 7)	4 (2–6)	16 (10–23)	15 (9–23)	22 (13–33)
	Lymph node (+) (*N* = 4)	1 (0–2)	7 (3–12)	13 (6–21)	11 (4–23)
6.1–10.0	Organ confined (*N* = 53)	**62 (55–68)**	**32 (26–38)**	**22 (17–29)**	**24 (17–33)**
	Extraprostatic extension (*N* = 28)	**32 (26–38)**	**41 (33–49)**	**47 (38–56)**	**38 (29–48)**
	Seminal vesicle (+) (*N* = 15)	5 (3–8)	20 (13–28)	19 (11–28)	27 (16–39)
	Lymph node (+) (*N* = 5)	1 (0–2)	6 (3–11)	11 (5–19)	10 (3–20)
>10.0	Organ confined (*N* = 8)	**46 (39–53)**	**18 (13–24)**	**11 (7–15)**	**12 (7–18)**
	Extraprostatic extension (*N* = 15)	**41 (34–50)**	**40 (31–51)**	**40 (30–52)**	**33 (22–46)**
	Seminal vesicle (+) (*N* = 10)	7 (4–12)	23 (15–33)	19 (10–29)	28 (16–42)
	Lymph node (+) (*N* = 8)	5 (2–8)	18 (9–30)	29 (15–44)	26 (12–44)

As in previous versions of the Partin tables,[4–6] PSA, biopsy Gleason score, and clinical stage contributed significantly to the prediction of pathological stage in the multivariable logistic regression. Risk of both extraprostatic extension and seminal vesicle or lymph node involvement increased significantly with successively higher categories of PSA, clinical stage, or biopsy Gleason score (p <0.001). There were several important exceptions to this. First, there was a lack of significant difference in risk of seminal vesicle or lymph node involvement between PSA categories 0–2.5 and 2.6–4.0 ng/ml (p = 0.507); however, this may reflect the small number of patients with this pathology outcome in the lowest two PSA ranges (n = 19). Also, in all cases, the nomogram predicts that patients in Gleason grade 8–10 do better that those in Gleason grade 4 + 3 = 7. This probably does not reflect the biology of these tumors, but rather reflects a selection bias inherent in studying only men who have undergone surgical treatment of their CaP. Most of the patients known to have high-grade disease were first screened (75%) with bone scan and CT scan to detect occult metastasis. Therefore, all patients discovered a priori to have T4 disease are excluded from analysis. The combination of the three preoperative variables predicted pathological stage better than any single variable.

The predicted probabilities from the multivariable logistic regression analysis and bootstrapped 95% confidence intervals are presented in the nomograms. The numbers within each cell of the nomogram represent the predicted probability of a given pathological stage based on the regression on the three preoperative variables. For example, a man with a preoperative serum PSA level of 2.7 ng/ml and a biopsy Gleason score of 3 + 3 = 6 and a non-palpable (Stage T1c) DRE has an 88% probability of organ-confined disease, an 11% chance of having extraprostatic cancer not invading the seminal vesicles or the lymph nodes, a 1% probability of having disease in the seminal vesicles, and a very low probability (close to 0) of having lymph node metastasis. A man with a PSA of 11.4 ng/ml and a biopsy Gleason score of 8 with a large palpable tumor (stage T2c) has only a 12% chance of organ-confined disease at surgery, a 33% probability of having extraprostatic extension, a 28% probability of having seminal vesicle involvement, as well as a 26% chance of lymph node metastasis.

Owing to a change in the biology of CaP or as a result of improved detection, men presenting with CaP today are more likely to have organ-confined disease.[35] An important point to note here, is the variability between different groups and even between different surgeons in the procurement of lymph nodes and the determination of lymph node metastasis. Certain researchers have discussed the need for extended lymph node dissection among men with CaP[38] and certain groups have demonstrated the predictive capability of even occult lymph node metastasis.[39,40] Allaf et al[41] have previously summarized the experience with lymph node dissection at Johns Hopkins Hospital. One surgeon routinely performed a limited lymph node dissection (mean 11.6 versus 8.9 nodes, p <0.0001). The extended lymphadenectomy detected more lymph node positive disease (3.2% vs 1.1%, p <0.0001). Thus, even within one institution, changing the limits of dissection might affect the numbers of patients with lymph node metastasis. Interestingly, when adjusted for fraction of total number of positive lymph nodes, the progression free survival for the patients undergoing extended dissection was better than those patients undergoing limited dissection. Longer follow-up will be necessary to determine whether these data will influence mortality.

Stage migration must be accounted for in the models which we use to predict the behavior of CaP, if we are to make accurate treatment recommendations for contemporary patients. We have used data from 5734 patients treated in the years 2000–2005 to develop an updated set of

Partin tables, which use preoperative serum PSA, clinical stage, and biopsy Gleason score to provide the estimated probability of various final pathological stages at RP. We found that, because of declining numbers of patients presenting with advanced-stage disease, combining clinical stages T2b and T2c into a single group generated a more robust and easy-to-use model. These improvements to the tables should make them even more useful to clinicians and patients alike.

Another notable change in the model is the absence of Gleason 2–4 disease. This phenomenon derives from a consensus among pathologists to avoid reporting Gleason pattern 2 on biopsies.[36] This is because Gleason pattern 2 tends not to be present in the peripheral zone of the prostate, but rather anteriorly in the transition zone. Almost all Gleason 2–4 disease on biopsy is upstaged once the entire gland has been removed, suggesting that Gleason 2–4 disease represents a sampling error.

Comparing the 2007 nomogram to the 2001 nomogram,[6] we see an overall trend towards the prediction of organ-confined disease. This trend is most apparent when examining the differences between probabilities of organ-confined disease among patients with high Gleason score (8–10) and advanced clinical stage (T2b/T2c). Contrary to expectation, the combined T2b/T2c group used in this work predicts more organ-confined disease than the 2001 tables predict for a pure T2c category. Examining the predicted probabilities for men with T2b disease from the 2001 tables, we see that for the increasing PSA categories, men with Gleason score 8–10 have probabilities of organ-confined disease are 34%, 23%, 18%, 13%, and 6%. The corresponding values from the current nomogram for men with clinical stage T2b/T2c and Gleason score 8–10 are 49%, 39%, 27%, 24%, and 12%. While the confidence intervals from these groups do overlap minimally, there is a trend toward a difference in pathological outcomes. Such a difference may have important implications regarding the management of advanced-stage, advanced Gleason score prostate cancer. Although many of these men in the past would have received radiation with adjuvant hormone therapy, with the belief that they had been detected with disease having likely spread outside the prostate, this cohort of patients in the modern era may actually be amenable to surgical cure.

CONCLUSIONS

PSA, DRE, and Gleason score are all reasonably good individual predictors of the pathological stage of prostate cancer. However, in combination, a far better prediction can be made. This is the basis of the Partin tables. As current trends in presentation and pathological stage in men newly diagnosed with CaP continue to evolve, it becomes necessary to build new models on more recent data. We have reviewed the individual contributions of PSA, DRE, and Gleason score in this chapter. We have also reviewed their combinations into the Partin tables and present a new set of tables based on data from men treated after the year 2000. Clinicians can use this nomogram, based on the large cohort of men with CaP treated at our institution, to counsel individual patients and help them to make important decisions regarding management of their disease.

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CHAPTER 5

The role of imaging techniques in the staging of suspected organ-confined disease

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INTRODUCTION

The detection of prostate cancer at an earlier stage and the variability of the disease course have made treatment decisions increasingly difficult, and the prognosis unpredictable, which is not great news for those treating the most commonly diagnosed non-cutaneous cancer in males.[1]

The main factors influencing treatment decision are the stage of the disease and in particular whether it is an organ-confined (T1/T2), locally advanced, or metastatic (T3/4) disease. To an extent this can be evaluated using digital rectal examination (DRE), prostate-specific antigen (PSA) level at presentation, the results of needle biopsy, and then consulting nomogram tables such as the Partin table. Only when these data have been correlated, and the patient assigned a particular risk level, can imaging contribute.

Imaging can provide information on local staging and has the potential to map tumor location, providing anatomical detail for surgical planning. It can also identify nodal and distant metastatic disease. Nevertheless, the precise role of radiology continues to be debated owing to cost, the advantages and disadvantages of different modalities, and the heterogeneity of reported accuracies. This chapter reviews the current status of the imaging techniques used in staging prostate cancer and new developments showing promise.

Although the prostate gland is visible using computed tomography (CT), ultrasonography (US), and magnetic resonance imaging (MRI), it is the latter that has the most important role in the accurate staging of organ-confined disease. Bone scintigraphy is useful in assessing bone marrow for metastatic spread. This chapter will focus primarily on MRI but will also discuss other techniques, such as the use of dynamic contrast enhancement in MRI and functional imaging with magnetic resonance spectroscopy (MRS). These have shown some promising results but as yet are not in routine use. A detailed knowledge of the radiological anatomy is essential for accurate staging. Figure 5.1 shows the anatomy, as depicted on CT, US, and MRI.

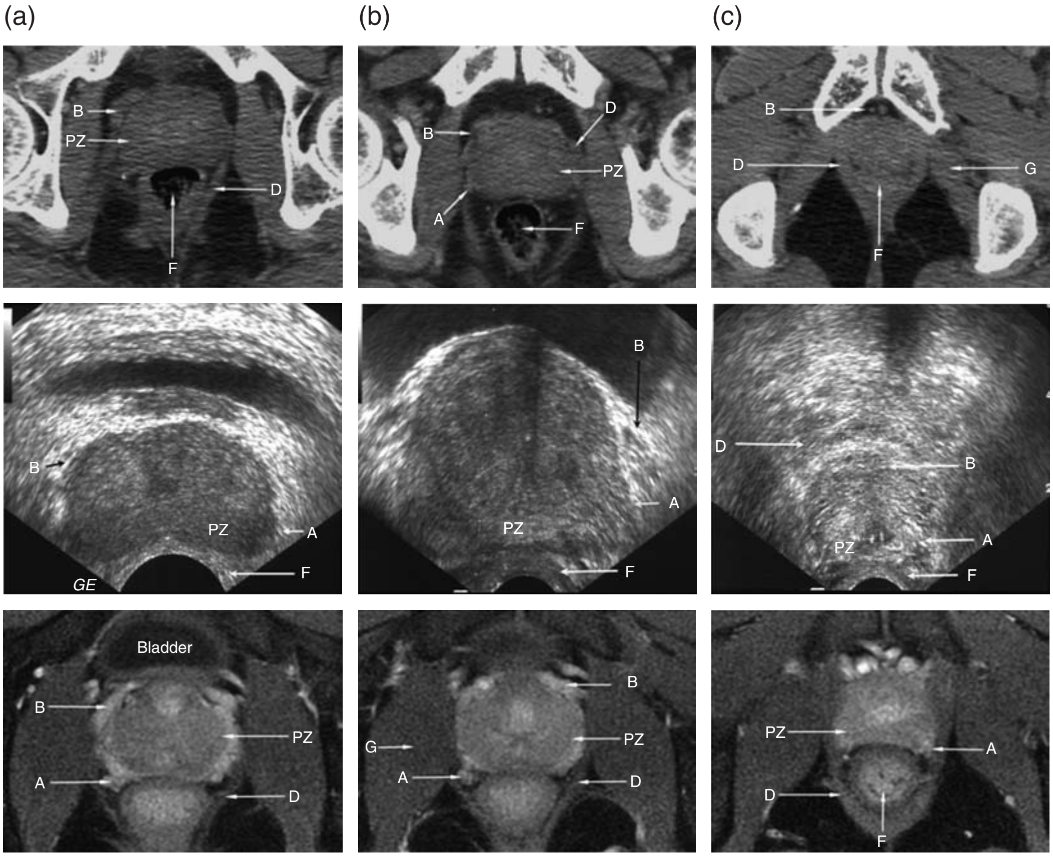

Figure 5.1 An appreciation of the anatomy is essential to accurately stage prostate malignancy on imaging. Comparative slices through the prostate using the different modalities are shown in an axial plane from the base (a), midzone (b), and apex (c) of the prostate. The order of the images are CT first, then TRUS, and MRI. The peripheral zone (PZ) is seen well with TRUS and T2-weighted MRI but not appreciated on CT. Important structures to note are the neurovascular bundles and the deep and superficial venous plexi. These structures are seen well on MRI and also appreciated on TRUS. CT poorly delineates the local periprostatic anatomy. A, neurovascular bundles; B, periprostatic venous plexus; C, prostatic fascia; D, levator ani; E, seminal vesicles; F, rectum; G, obturator internus; PZ, peripheral zone.

STAGING

The goal of staging is to define the local, regional, and systemic extent of the disease. Prostate cancer is staged using two main systems: the Jewett–Whitmore was the first widely used system but has now largely been replaced by the TNM system. The TNM system was initially devised by Pierre Denoix in the 1940s and can be applied to almost any cancer type or site. It describes the local stage (T), the nodal status (N), and metastatic disease (M). The first TNM system for prostate cancer was proposed in 1975 and has been revised

Table 5.1 TNM staging of prostate cancer (2002)

T – Primary tumor	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Clinically inapparent tumor not palpable or visible by imaging
T1a	Tumor incidental histological finding in 5% or less of tissue resected
T1b	Tumor incidental histological finding in more than 5% of tissue resected
T1c	Tumor identified by needle biopsy (e.g. because of elevated prostate-specific antigen [PSA] level)
T2	Tumor confined within the prostate[a]
T2a	Less than one-half of one lobe involvement
T2b	Greater than one-half of one lobe involvement
T2c	Bilateral involvement
T3	Tumor extends through the prostatic capsule[b]
T3a	Extracapsular extension (unilateral or bilateral)
T3b	Tumor invades seminal vesicle(s)
T4	Tumor is fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles, or pelvic wall
N – Regional lymph nodes[c]	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
M – Distant metastasis[d]	
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis
M1a	Non-regional lymph node(s)
M1b	Bone(s)
M1c	Other site(s)

[a] Tumor found in one or both lobes by needle biopsy, but not palpable or visible by imaging, is classified as T1c.
[b] Invasion into the prostatic apex, or into (but not beyond) the prostate capsule, is not classified as T3, but as T2.
[c] Metastasis no larger than 0.2 cm can be designated pN1mi.
[d] When more than one site of metastasis is present; the most advanced category should be used.

in 1992, 1997, and most recently in 2002 (see Table 5.1).

The value of the TNM system, which uses both clinical and pathological information, is that it can be translated into expected patient outcome and helps plan the treatment strategy. However, pathological stage is recognized as the single most powerful prognostic variable,[2] but by its very nature requires the prostate to be removed. The aim of imaging is to try to closely mirror pathological staging.

WHICH IMAGING MODALITY SHOULD BE USED?

The imaging modality used depends on whether local, regional, or metastatic extension is being sought. In assessment of regional and metastatic disease, CT, MRI, and nuclear medicine studies all have a role to play. For local disease, transrectal ultrasound (TRUS) and MRI are the mainstay modalities. CT has very poor sensitivity and specificity for assessing local disease and its role is really in defining nodal disease and distant metastases.[3–5]

LOCAL STAGING

Transrectal ultrasound

The primary role of TRUS is in targeting prostatic biopsies[6] and its role in local staging has always been controversial. More recently, its accuracy has been further undermined by the downward stage migration of the disease. Historically, some 60–70% of cancers were seen as hypoechoic nodules on TRUS (Figure 5.2), but in contemporary practice the vast majority are isoechoic, non-specific, or invisible on TRUS. Naturally, this will hinder its value in staging, particularly with T1/T2 tumors. However, if the tumor is visible, capsular penetration or local extension may be evaluated.

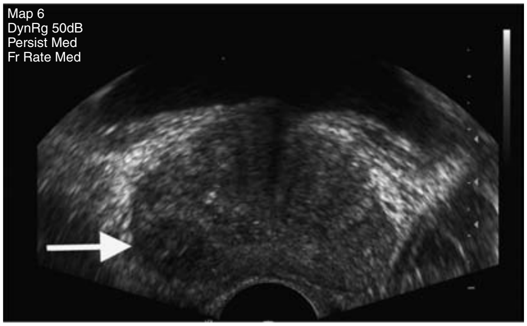

Figure 5.2 TRUS image showing a focal area of hypoechogenicity within the right peripheral zone (white arrow). Prostate carcinoma was confirmed on biopsy. It has broad contact with the capsule suggestive of extracapsular extension, but TRUS is relatively poor for local staging.

Extracapsular extension

Extracapsular extension (ECE) is best evaluated in the transaxial plane and is suggested by a hypoechoic area that causes distortion and irregularity of the normal contour of the prostate (Figure 5.3). The overall accuracy for ECE has been quoted as 46–84%; however, a lot of these studies are relatively old. A study in 2002 by Mearini et al, using histological correlation, quoted a value of 50%.[7] Values for sensitivity and specificity vary widely between studies – sensitivity between 23 and 86% and specificity from 46 to 94%.[8–10]

Seminal vesicle invasion

Seminal vesicle invasion (SVI) is best seen on sagittal views and is suggested by a loss of the normal tapering of the seminal vesicles near the

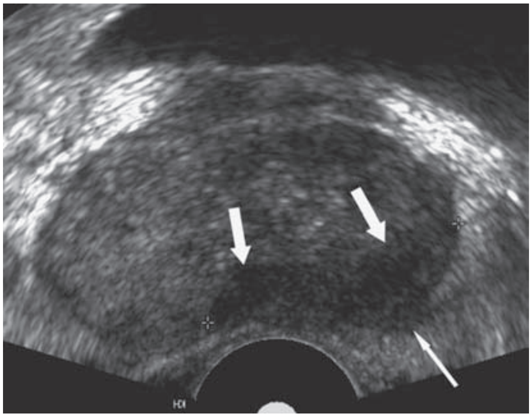

Figure 5.3 Extensive hypoechoic area within the left peripheral zone that crosses the midline (thick arrows). Hypoechoic changes are inseparable from adjacent left neurovascular bundle (thin arrow) suggesting T3 disease. Biopsy confirmed prostatic carcinoma with a Gleason score of 4 + 5 and perineural invasion.

Table 5.2 Diagnostic and staging using transrectal ultrasound in prostate cancer

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Advantages of TRUS for local staging

- It is relatively cheap and widely available
- Guidance for transrectal biopsy

Disadvantages

- Wide variation in the quoted sensitivity and specificity
- Operator dependence

Current practice

TRUS is mainly used as a means to guide prostatic biopsy. There is some evidence to suggest that it can improve the local T staging of tumors and diagnose T2 disease

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prostatic base. In advanced SVI, low-echogenicity tumor can be seen extending into the vesicles from the prostate. The prediction of SVI again has widely varying sensitivity and specificity, at 20–92% and 65–100%, respectively.[11] Table 5.2 summarizes the current diagnostic and staging value of TRUS in CaP.

Magnetic resonance imaging

With its superior soft tissue resolution and faithful anatomical representation, MRI is the best modality for assessing the local T stage; however, widely discrepant results have been reported in the literature: some can be explained by technical factors, in particular the choice of imaging coils, but others reflect the difficulty in analyzing local disease and demonstrating microscopic extracapsular spread.

Coil types – does it matter?

The idea of using an endorectal coil (ERC) instead of a pelvic phased array coil (PPA) is to improve spatial and contrast resolution by imaging closer to the prostate. This is true for the posterior aspect of the gland, but unfortunately a signal from the anterior aspect is not well received if the ERC is used alone. Therefore, the apex of the gland, where the peripheral zone (PZ) wraps anteriorly, cannot be well seen.[12] This problem is overcome by using the ERC in conjunction with a PPA coil to obtain a good signal from the anterior gland.

The use of an ERC also has a number of drawbacks. First, the patient experiences discomfort with insertion of the probe and air insufflation of the cuff in the rectum. Secondly, it requires that a suitably qualified member of staff be present to insert the probe. ERCs are also susceptible to near-field artifact (signal hyperintensity surrounding the coil) and can cause structural deformity of the PZ, making image interpretation difficult.[13] New software on the latest scanners applies an analytical correction of the reception profile of the ERC to counteract this artifact.[14] For the routine use of ERCs to be warranted they would have to provide significantly more accurate staging but there are conflicting reports in the literature. A meta-analysis by Sonnad et al[15] showed that receiver operator characteristic (ROC) curves for different coil types were not significantly different. This conflicts with a meta-analysis by Engelbrecht et al[16] that suggested that endorectal coils improved staging accuracy. Hricak et al[17] have also shown an improved accuracy of endorectal coils over PPA of 77% compared with 68%. This would appear to make an argument for the use of ERCs but the question of whether this is a significant overall improvement has still not been answered. Most institutions are currently only using PPA coils.

Appearance of cancer on MRI

In common with most cancers, prostate cancer is seen as a relatively low signal on T2-weighted studies (reflecting the high ‘free’ water content of malignant tissue), although rarely it can also be an increased or heterogeneous signal.[18,19]

As most prostate cancers arise within the PZ, prostate cancer foci should theoretically be readily visualized on MRI within the homogeneous high signal intensity background of the PZ on T2-weighted images. In practice, this is not always the case. The tumor may not be visible at all,[20] or, alternatively benign prostatic conditions that are common in this age group (e.g. benign prostatic hyperplasia [BPH], prostatitis) may mimic prostate cancer. Occasionally, the tumor is so large that the normal PZ is completely replaced, and the resulting poor contrast resolution makes the tumor difficult to demonstrate. Likewise, if the normal high-signal PZ is compressed by an enlarged transitional zone (TZ) secondary to BPH, it can appear of low signal, making the detection of tumor very difficult.

Tumor detection within the central (CZ) and transitional zones is especially challenging as the low signal tumor foci are lost within the heterogeneous signal due to BPH. Focal homogeneous areas of decreased signal on T2-weighted images with ill-defined margins have been reported as suggestive of a cancer in the TZ[21,22] but this is not entirely specific. Lastly, post-biopsy artifact (representing hemorrhage) is a further mimic of prostate cancer, appearing as a low signal focus on T2 studies. Review of the T1 images should help, as blood products tend to be a high signal on these, but it is recommended that imaging is not performed until at least 3–4 weeks after the biopsy.[23] Although these confounders interfere with image interpretation, well-conducted MRI scans can contribute to the management of prostate cancer and can assist the risk-stratification of high-risk groups. Figure 5.4a–d shows different stages of cancer on MRI.

Extracapsular extension on MRI

Table 5.3 Features suggestive of extracapsular extension on MRI

Irregular or smooth bulging of the capsule
Capsule signal disruption
Periprostatic fat infiltration
Length abutted by low signal intensity greater than 12 mm
Retraction of capsule
Thickening of the capsule
Obliteration of the rectoprostatic angle

There is a wide range of values for the accuracy of MRI in staging local disease. The major stumbling block is the inability to define early ECE well, with sensitivities and specificities being quoted in the literature as 38–80% and 50–97%, respectively.[16,24,25] This can be explained by the lack of reliable imaging features that can consistently identify ECE. Indeed Engelbrecht et al[16] found more than 20 described variables in the literature. Many of these were poorly defined and the most useful are listed in Table 5.3.

Using these variables to obtain an overall impression, experienced radiologists can identify ECE with a sensitivity of 68% and specificity of 72%, with the most specific single criterion being asymmetry of the neurovascular bundles (see Figure 5.4d) with a sensitivity of 38% and specificity of 95%.

Seminal vesicle invasion

Seminal vesicle involvement denotes T3b disease with higher likelihood of tumor recurrence and treatment failure. The prevalence of SVI is reported as between 4 and 12%.[26–28] The sensitivity and specificity of MRI for the detection of SVI are in the range 50–71% and 66–95%, respectively.[25,29–33] Features that suggest SVI include low signal intensity in the seminal vesicle (Figure 5.5), particularly medially, lack of preservation of the normal architecture (which together gives the highest sensitivity and specificity), expansion of the ejaculatory ducts, and obliteration of the angle between the prostatic gland and seminal vesicle. It is recognized that other benign conditions, such as hemorrhage,

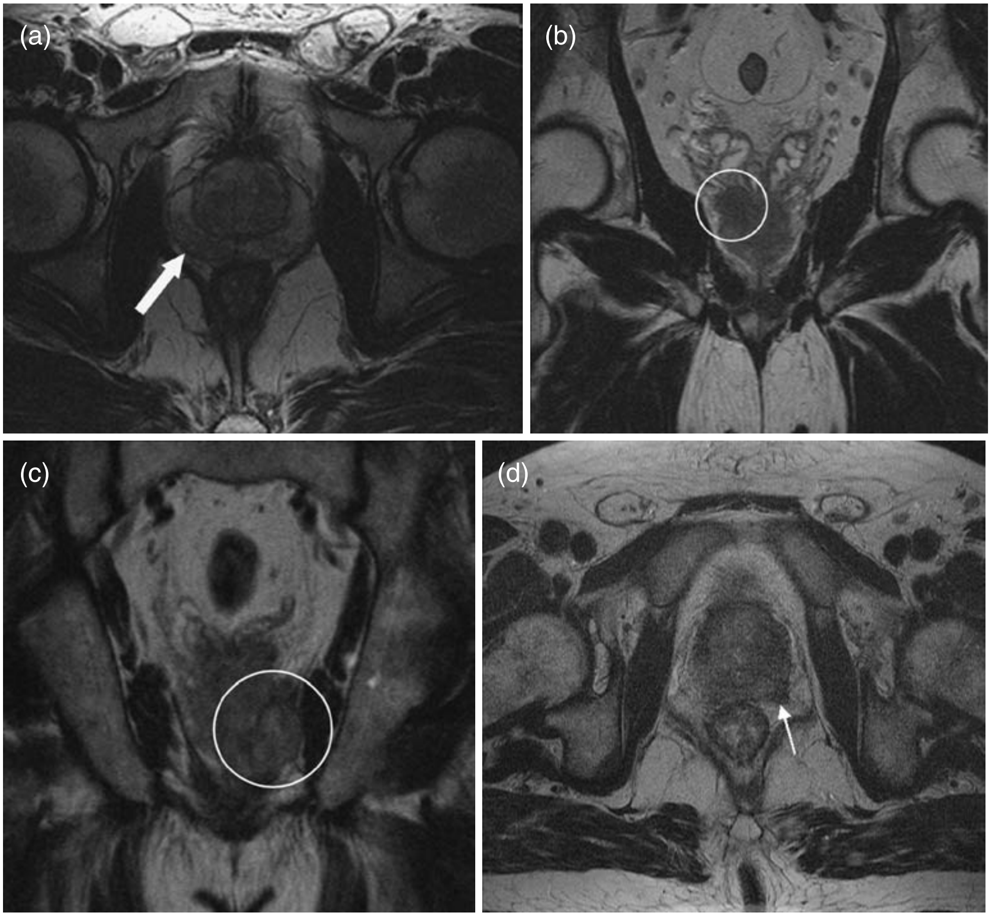

Figure 5.4 High-resolution T2-weighted MRI images through the prostate gland demonstrating the MRI findings with gland confined and locally extensive prostate cancer. (a) Low signal in the right peripheral zone (arrow), but the capsule is seen to be intact. The appearances are of a T2 prostate cancer. (b) There is a focal area of low signal within the right peripheral zone extending through the capsule and invading the seminal vesicle (white circle). This is a stage T3b cancer. (c) Abnormal soft tissue in the left peripheral zone (white circle). This extends outside the capsule and reaches up to the obturator internus muscle. The staging is T4. (d) This axial image shows enlargement of the left neurovascular bundle (arrow), indicating T3a disease.

scarring, amyloid, and post-radiotherapy change can result in low signal change in the seminal vesicles. Table 6.4 summarizes pros and cons of MRI in local staging of prostate cancer. Figure 5.6 demonstrates the ability of MRI to detect both SVI and regional nodal involvement.

REGIONAL STAGING

The presence of a single positive lymph node changes a patient's stage from local to systemic disease and the likelihood of lymph node deposits at the time of presentation is closely related to the grade and clinical stage of the tumor. For example, a patient with a well-differentiated T1a tumor has a negligible probability of having lymph node metastases,[34] whereas a patient with a poorly differentiated T3 tumor has a 68–93% probability. Therefore, investigation for nodal metastases can be risk-stratified.

Lymph node assessment using CT or MRI is therefore often performed but the quoted accuracy for either technique has varied widely. For CT, the sensitivity and specificity are in the range 25–100% and 44–100%, respectively,[35,36] and for MRI 89–100% and 77–100%, respectively.[37,38]

This is partly because the diagnosis of lymph node involvement on CT or MRI is primarily based on size. A short-axis diameter of >1 cm is taken as indicating involvement. Nonetheless, this cut-off results in a significant number of false negatives. In addition to the size, the shape and appearance of nodes are alternative but less-specific markers for disease involvement, as are the signal intensity and enhancement characteristics. However, none of these factors will identify micrometastasis or early lymph node involvement.

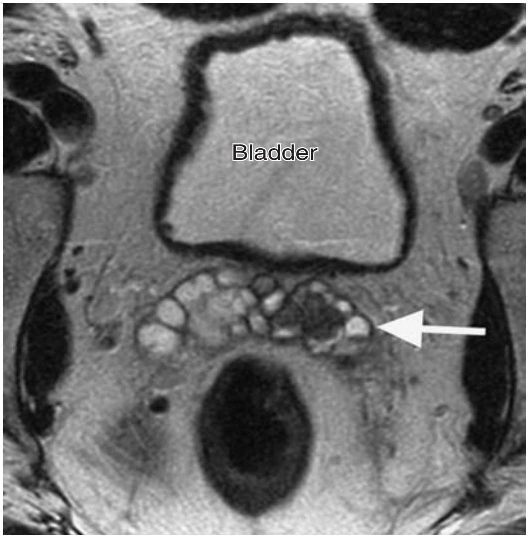

Figure 5.5 T2-weighted MRI image showing low signal change within the left seminal vesicle (white arrow). This indicates invasion of the seminal vesicle, suggesting T3b disease.

Table 5.4 Pros and cons of MRI in local staging of prostate cancer

Advantages of MRI for local staging
- Best spatial and contrast resolution
- Able to define local anatomy and can influence surgery
- Readily available

Disadvantages
- Contraindications
- Cost
- Post-biopsy hemorrhage

In a bid to try to improve accuracy, recent work using superparamagnetic nanoparticles (SPIOs) has shown promise. This is an iron-based compound that is taken up by normal lymph tissue 24–36 hours after intravenous injection[39] but not by tumor cells. On post-contrast images, normal functioning nodes are seen as very low signal intensity on T2-weighted images, whereas metastatic nodes remain unchanged or become heterogeneous in signal.

Harisinghani et al compared the sensitivity of MRI with lymphotropic SPIOs with that of conventional MRI in 80 patients, correlating with histopathological findings, and found the overall sensitivity to be markedly improved: 90.5% compared with 35.4%.[40] They were also able to detect smaller involved nodes in the range 5–10 mm, which is comparable with positron emission tomography (PET), whose range is 6–10 mm.[41] A study has also been performed using SPIOs and a 3 tesla (3T) magnet by Heesakkers et al,[42] showing that SPIOs can be used at this field strength. They also postulated that at this magnet strength it may well be possible to detect < 5 mm metastases. These results are at least intriguing, but need to be replicated in routine practice (Table 5.5).

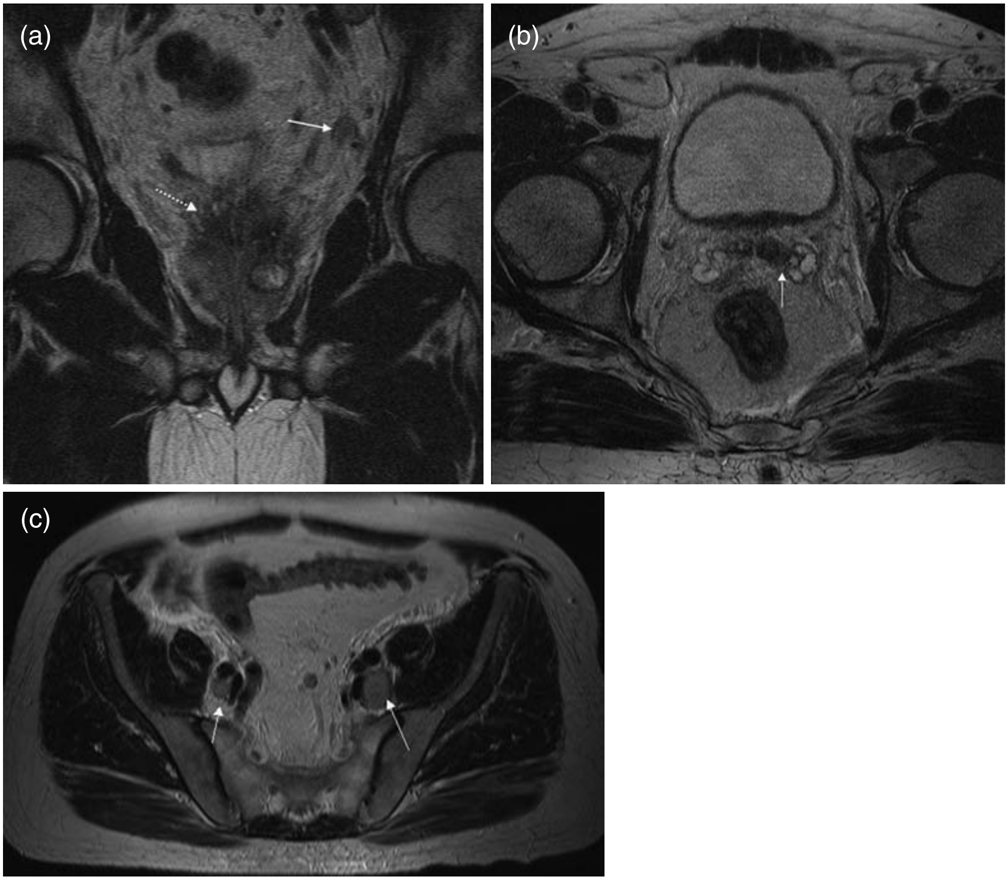

Figure 5.6 This montage demonstrates locally extensive and metastatic prostate cancer, in a man with Gleason 5 + 5 cancer on biopsy and PSA of 14.3 ng/ml. (a) Coronal T2 view showing an irregular outline to the base (hatched arrow) with an enlarged left-sided obturator node (solid arrow). (b) Left seminal vesicle invasion is confirmed on the axial T2 view (arrow). (c) The pelvic views show bilateral enlarged iliac lymphadenopathy (arrowed).

DISTANT SPREAD

CT, MRI, and bone scintigraphy all have roles in assessing for distant metastatic disease.

MRI

When reviewing the pelvic MR images, the bone marrow should also be assessed for areas of low signal, particularly on the T1-weighted images, which might indicate the presence of bony metastatic spread.

Bone scintigraphy

Bone scintigraphy is the most widely used radionuclide investigation and is a very sensitive method for detecting metastatic deposits within the skeleton. As with local extension and lymph node involvement, the probability

Table 5.5 Lymph node involvement

- Chances of nodal metastases related to tumor grade and clinical stage
- CT and MR varying sensitivity and specificity
- Metastatic involvement conventionally judged on size (>1 cm) and shape (round)
- SPIO – involved nodes do not take up particles and thus do not lose signal:
  improves sensitivity over conventional MR (90.5% vs 35.4%)
  allows detection of smaller metastases (5–10 mm)

of bone deposits is also stage and PSA dependent. The value of bone scans in patients with PSA levels less than 20 ng/ml and certainly less than 10 ng/ml is a matter of debate. Oesterling et al found that less than 0.5% of scans were positive when the PSA level was less than 10 ng/ml. Furthermore, only 1% of men had positive scans if the PSA was 20 ng/ml or less.[43] Positive scans are more common in those with higher PSA levels and higher Gleason grades (Figures 5.7a and b).

Although highly sensitive, with a false-negative rate of less than 1%, the specificity of radionuclide bone scan is poor. The specificity is lower in those with a low pre-test probability of bone metastasis. The main reason for high false positives in these patients with lower PSA values is that the characteristic or diffuse multiple metastatic deposits are not seen. Instead, the examination detects other and more common benign conditions. Degenerative arthropathy (Figure 5.8a), healing fractures, and metabolic diseases (e.g. Paget's disease – see Figure 5.8b) are common in this age group and can all simulate metastatic disease.[44] All these pathologies may give rise to a positive scan and, as such,

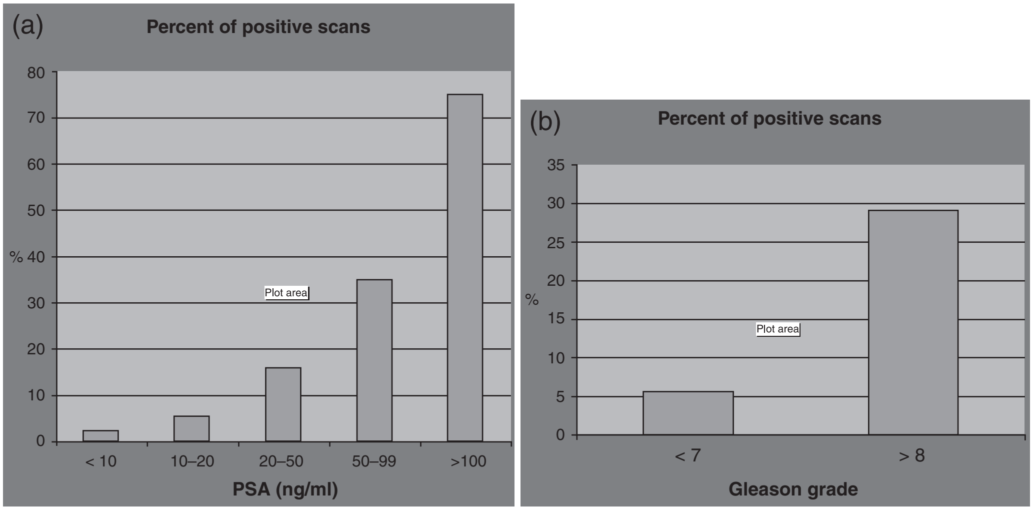

Figure 5.7 Graphs showing the percent of positive bone scans vs PSA (a) and Gleason grade (b). It can be seen that the PSA has to be >20 and the Gleason grade >7 for a significant number of scans to be positive. (Reproduced from Abuzallouf F, Dayes I, Lukka H. Baseline staging of newly diagnosed prostate cancer: a summary of the literature. J Urol 2004; 171(6 Pt 1):2122–7, with permission.) It should be remembered that all symptomatic patients should be scanned whatever their PSA or Gleason grade.

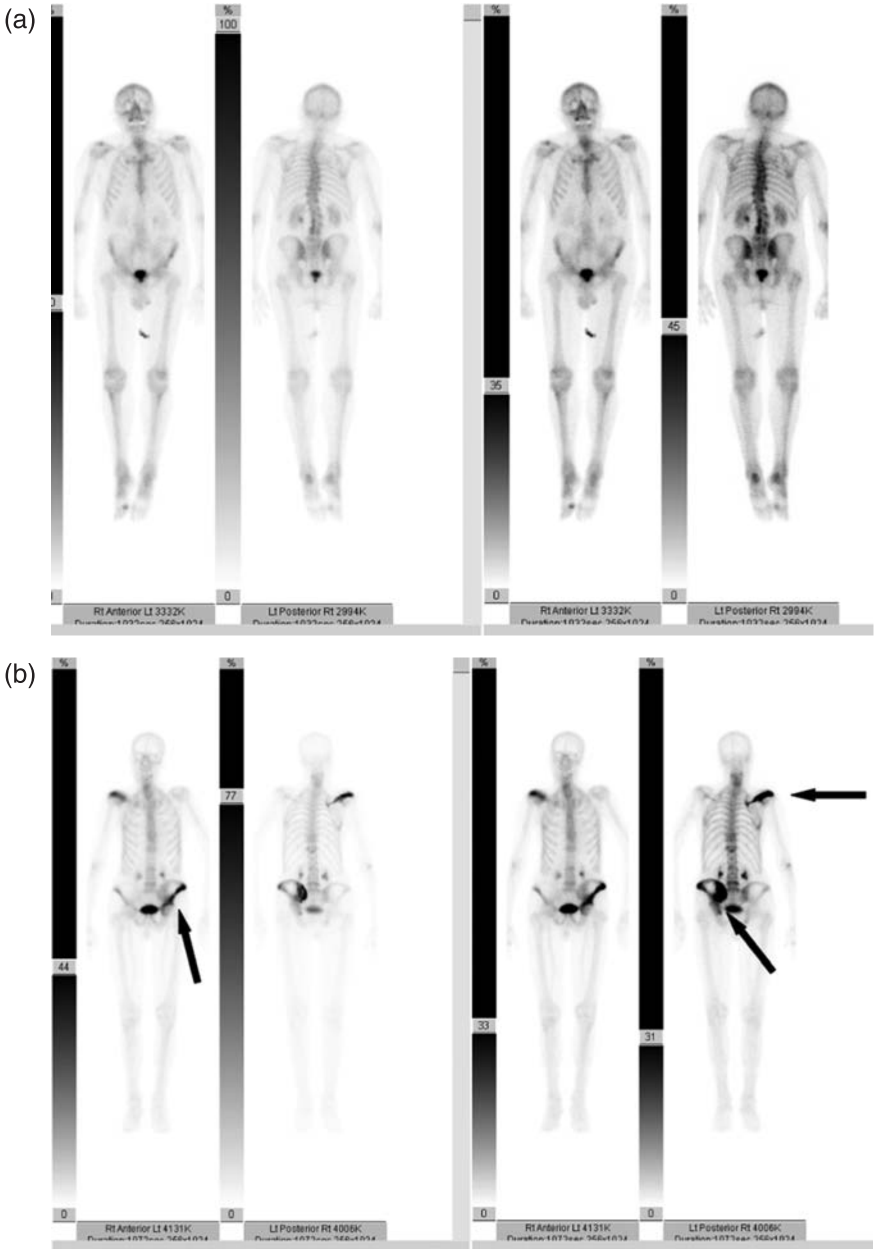

Figure 5.8 (a) Bone scan showing diffuse uptake in the spine around the thoraco-lumbar scoliosis. The cause in this case was degenerative disease of the lumbar vertebra, but metastatic disease can present with similar appearances. Degenerative disease is the commonest cause of false-positive or indeterminate bone scintigraphy. (b) There is marked uptake seen within the left iliac wing and scapula (arrowed). Owing to the poor specificity of bone scans, the cause for this abnormality cannot be ascertained on bone scan alone. In this case, the diagnosis was Paget's disease.

further investigations need to be performed. Correlation with plain radiography may help resolve the imaging uncertainty. If not, CT or MRI scans are necessary to further evaluate the bones and marrow respectively (Figures 5.9a and 5.9b).

WHEN SHOULD IMAGING BE USED?

The common themes of the discussions above are the good, but not perfect, accuracies of the various imaging modalities for prostate cancer staging, and that the likelihood of locally advanced disease or metastasis can be risk-stratified. Thus, imaging strategies can be formulated and guided by the pre-test probability of local and/or metastatic disease. A similar strategy has been proposed by D'Amico et al.[45]

Imaging is then employed according to a pre-treatment work-up plan that is decided locally. Figure 6.10 gives one such imaging pathway used in our practice: however, there are no hard and fast rules.

NEW DEVELOPMENTS

Tesla scanners (3T)

Higher-strength MR magnets increase the signal to noise ratio (SNR), allowing either improved spatial or temporal resolution. Increasing magnet strength from 1.5T to 3T should improve the SNR by a factor of 2.[46] 3T magnets should allow scanning without ERCs while providing images of a similar quality to those obtained with an endorectal coil at 1.5 T. However, even better spatial resolution is obtained if combined PPA and endorectal coils are used.[47,48]

Futterer et al[49] looked at the local staging accuracy of 3T endorectal MRI. They found an accuracy of 94%, a sensitivity of 88%, and a specificity of 96%. There is no doubt 3T and higher field strength scanners improve spectral and temporal resolution, but there are only a few units in place in the UK. Current research work performed on 3T magnets show very promising results and, as current safety studies show no ill-effect, these are likely to replace the conventional 1.5 T scanners in the future.

Dynamic contrast-enhanced MRI

(Figure 6.11a–d)

Several studies have shown dynamic contrast-enhanced MRI significantly improves detection of cancer that is confined to the prostate gland. The sensitivity when compared with T2-weighted sequences increased from 57% to 73%, with no reduction of specificity of 83%.[50] Other studies confirm this finding.[51–53]

Improvements in detecting extracapsular spread (84%) and seminal vesicle involvement have also been reported (97%).[54]

It is generally accepted that prostatic MRI using dynamic contrast imaging and an endorectal coil improves tumor detection, capsular penetration, neurovascular bundle involvement, and seminal vesicle involvement when compared with non-contrast-enhanced MRI. Tumor detection is more accurate in the peripheral zone than in the transitional zone.

Functional MRI

Normal MR imaging of the prostate uses morphology alone to assess cancer, which results in a decreased accuracy due to the fact that many benign processes can imitate malignancy. Novel MR techniques to look at the function of prostatic cancer and of the normal prostatic tissue are currently a hot topic in the hope of increasing the specificity, but, more importantly, of increasing the sensitivity in diagnosing prostate cancer.

MR spectroscopy

MRS essentially measures metabolic activity. The differences in production and consumption

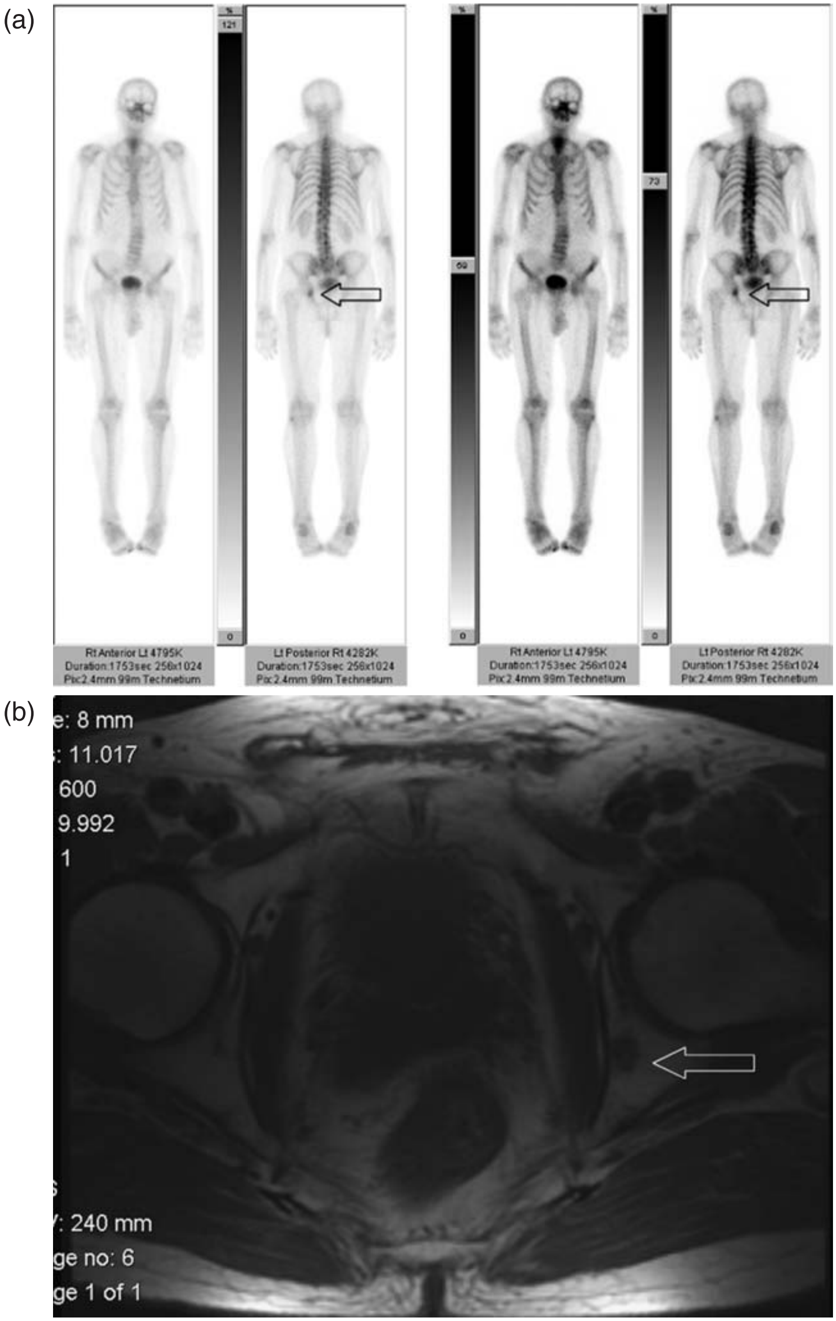

Figure 5.9 (a) Increased uptake is seen around the left hip joint (arrow on the posterior images). Bone scan cannot accurately differentiate between degenerative change or metastatic disease. This patient had a grade T2 prostate cancer and a PSA level of 13 ng/ml. (b) This is a T1-weighted axial MRI image of the same patient. There is a low signal focal abnormality seen within the left superior acetabulum (open arrow). Appearances on MRI are consistent with a metastatic deposit.

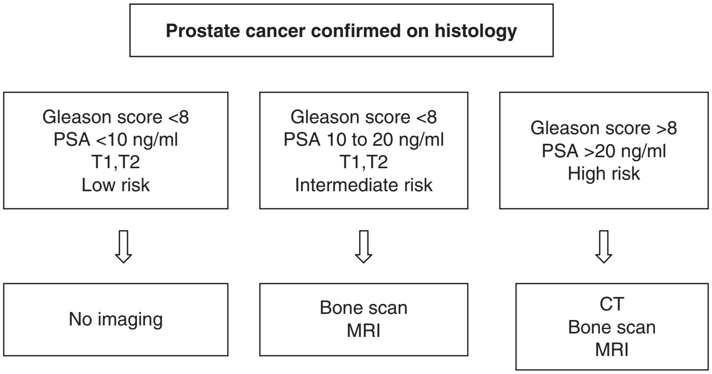

Figure 5.10 Suggested pathway to guide the choice of radiological investigation.

of creatine, choline, and citrate in normal tissue vs cancerous tissue are detected by MRS, and MRS complements MRI. When used together, better tumor localization and accuracy for predicting the presence of extracapsular spread are achieved.[55]

However, the data are conflicting and the true value of MRS is yet to be resolved. At present, MRS is probably more useful for the detection of cancer in previously treated prostate glands (e.g. ablative techniques) where post-treatment change obscures cancer on conventional MRI techniques.

Diffusion-weighted imaging (DWI)

DWI looks at the diffusion of free water within a tissue. It is a technique that is widely used in neurological imaging. Decreased diffusion occurs in highly cellular areas such as tumors or areas of cell swelling following the loss of energy-dependent sodium pumps, such as is seen in infarcted tissue.

It has been shown that prostate cancer does have lower diffusion than non-malignant tissue using an endorectal coil at 1.5 T;[56] however, there was significant overlap in individual values between normal and abnormal tissues. A further study by Pickles et al,[57] using a phased array coil and 3T magnet, also showed significantly lower diffusion values for tumor than for normal PZ. Again there was a considerable overlap of values between patient tissue types and it is not possible to quantify the benefits of this technique at present.

Other functional imaging techniques

Capromab pendetide (ProstaScint)

ProstaScint is a murine monoclonal antibody conjugated to an indium-labeled chelator that is directed towards prostate-specific membrane antigen (PSMA), a glycoprotein chiefly expressed by prostate epithelial cells. Although this imaging technique has been used in the initial staging of prostate cancer, it seems to be most useful in the follow-up of patients with probable relapse and rising PSA, particularly when images are fused with either MR or CT to help with anatomical localization.[58,59]

PET-CT

Functional imaging with [^{18}F] 2-fluoro-D-deoxyglucose (FDG) has proved invaluable in

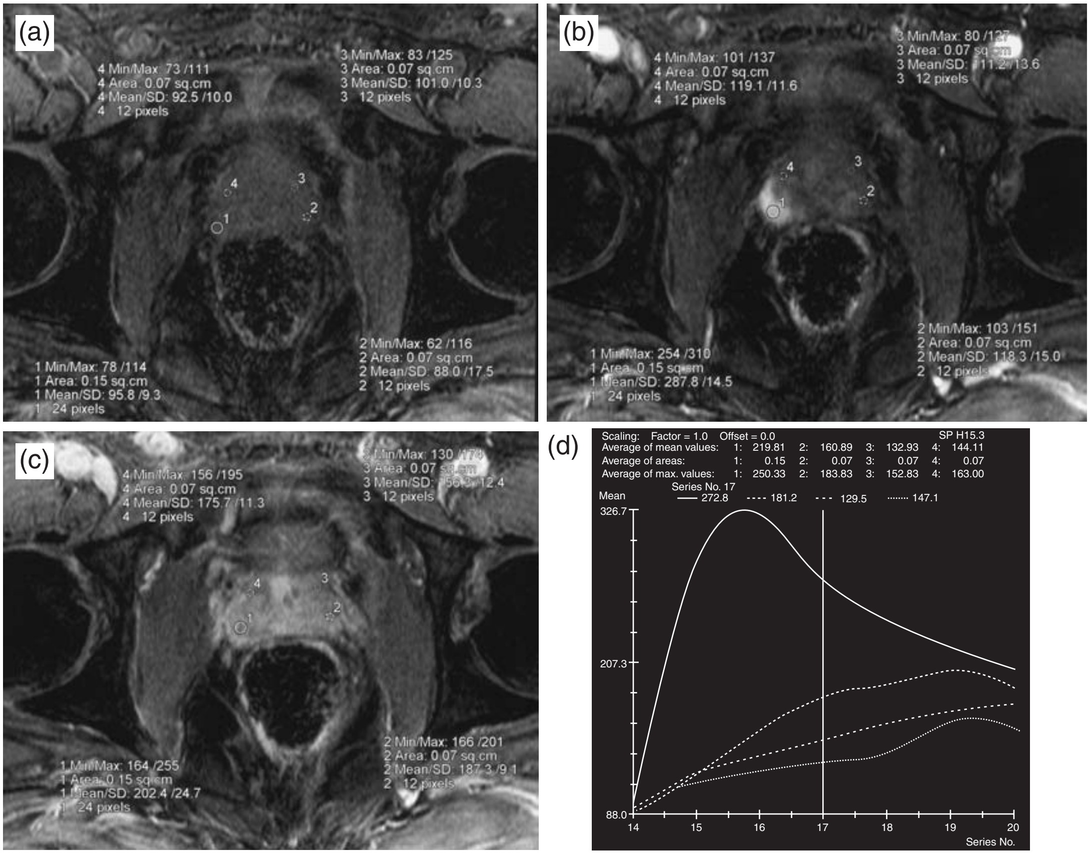

Figure 5.11 Dynamic contrast-enhanced MRI and associated graph of enhancement pattern. (a) The precontrast image. Four regions of interest (ROI) are chosen. Region 1 is placed over the area of suspected carcinoma. Regions 2, 3, and 4 are placed over presumed normal peripheral zone. (b and c) Early and late phase enhancement following gadolinium administration. In the early phase there is marked enhancement of region 1 compared with the other ROI, which then washes out more rapidly than the other regions (c). This finding is typical for a carcinoma and is shown graphically in (d).

the staging of certain malignancies, such as lung and colorectal cancers; however, results in prostate cancer have been disappointing. This is partly due to the renal excretion of FDG as well as limited sensitivity for the disease. It also performs more poorly than bone scintigraphy in assessment of the bone metastases.[60] The use of other agents, such as acetate, choline, or methionine, may prove more successful and they are currently under investigation.

THE FUTURE

Currently, MRI is the most accurate imaging test for primary staging of prostate cancer, but it remains an imperfect tool. As functional techniques evolve, the role of TRUS biopsy to diagnose prostatic cancer may need to be readdressed. Although we are several years away from even contemplating replacing biopsy with MRI, some studies suggest we are heading in this direction. It should be borne in mind that much of the current research has been performed at a limited number of institutions with very experienced observers and it remains to be seen whether these can be replicated if these techniques are instituted more widely. TRUS and biopsy itself is also an evolving field. The extended biopsy protocol is widely accepted[61] and achieves very high sensitivities (over 90%) that cannot be matched by MRI. Nevertheless, the emergence of new MRI and other functional techniques is fascinating and is likely to radically improve if not revolutionize imaging of localized prostatic cancer.

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Part 2: Technical considerations

CHAPTER 6

Anesthesiological care during and after radical prostatectomy

Miles A Goldstraw and Peter Amoroso

INTRODUCTION

Radical prostatectomy has been the gold standard treatment for clinically localized prostate cancer for over 30 years. Walsh and Donker were the first to describe anatomical radical retropubic prostatectomy (RRP),[1] and it has been continuously refined since that time in an attempt to decrease morbidity and mortality. More recently, a greater change has taken place with the development of minimally invasive techniques for radical prostatectomy. In particular, laparoscopic prostatectomy (LP) and robot-assisted laparoscopic prostatectomy (RALP) have gained increasing popularity, with these techniques offering purported benefits of reduced blood loss, decreased pain, and early mobilization with similar oncological efficacy. Early data may even suggest an improvement in functional outcome, including continence and erectile dysfunction.[2] However, the learning curve for these procedures is quite considerable and often results in prolonged operative times. This fact, in combination with the specific requirements of laparoscopy – namely, gas insufflation with head-down Trendelenburg tilt – results in a unique set of physiological demands on the patient.

PATIENT SELECTION

Patients attending for radical prostatectomy are typically middle-aged to elderly men. These men often have a number of comorbidities. The skill of the anesthetist is in recognizing those disease states that are chronic and stable compared to those which are deteriorating: the latter will need particular attention preoperatively in order to reduce overall risk. Common presentations include cardiovascular disease, respiratory disease, and/or features of the metabolic syndrome (central obesity, impaired glucose tolerance, and hypercholesterolemia). Ideally, these problems will have been detected at the pre-admission clinic and given sufficient time to be addressed. Fortunately, prostate cancer tends not to be a disease process needing emergency treatment. In fact, the current trend to wait 6 weeks following biopsy before undertaking surgery provides the perfect opportunity to improve patient fitness.

There are few true contraindications to LP and RALP, but these include disturbances of coagulation and/or elevated intracranial pressures. Relative contraindications include congestive heart failure, valve failures, severe chronic obstructive pulmonary disease, elevated intrapulmonary shunt, and ventriculoperitoneal shunt.[3] The American College of Cardiology and American Heart Association published guidelines for assessing patients with cardiovascular disease about to undergo non-cardiac surgery.[4] At present we are not performing RALP on those patients with significant cardiorespiratory disease. The combined effect of head-down tilt, pneumoperitoneum, and prolonged surgery make this form of surgery potentially high risk, although other groups consider it the method of choice since open surgery will also be challenging in this group. Obesity is not a significant problem for the operating surgeon when using the minimally invasive approach. However, obesity is a significant problem for the anesthetist. In general, obese patients often have a reduced lung function and are prone to develop postoperative respiratory complications. Recent evidence has suggested that overweight patients (body mass index [BMI] = 25–30) have a significantly impaired arterial oxygenation ($A_{a-}DO_2$) during laparoscopic surgery with Trendelenburg position.[5] This is hardly surprising and it would make sense for the overweight patient to achieve some weight reduction and fitness improvement ahead of surgery.

The preoperative work-up is the ideal opportunity to achieve optimum fitness and motivation, adjust the diet (adding in nutrients as considered appropriate), and achieve maximum patient and family information and education; the diagnosis of cancer will have profound effects on every man and he will require a great deal of support and advice. This can be a crucial component of the rapport developed with the anesthetist in the preparatory phase. The authors have evolved a role in working patients up for their operation, achieving significant weight and anxiety reduction in this difficult period. The situation becomes more complex if the patient wishes to discuss different treatment options in addition to the surgical removal of the prostate. Once again, the anesthetist with urological expertise is well placed to help the discussion progress. Whichever treatment choice is selected, there is no doubt that there is a great benefit to the physical and mental well-being of the patient if he focuses on fitness and a healthy diet.

ANESTHESIA

Anesthesia for the patient undergoing LP or RALP can be performed under both regional and general anesthesia and often a combination of both. Good muscle relaxation is necessary for the prolonged periods required. Epidural and subarachnoid blockade provide excellent operative conditions for laparoscopic surgery with a reduced blood pressure, low muscle tone, and high-quality analgesia. Full general anesthesia has the advantage of complete neuromuscular blockade using non-depolarizing muscle relaxants. These drugs can be used as part of a balanced anesthetic technique incorporating relaxation, analgesia, and sleep. In the authors' experience, the use of combined local and general techniques assures the advantages of both techniques with minimal side effects. Good operative conditions with a light general anesthesia and epidural blockade lend themselves well to prolonged surgery under these conditions.

The process of general anesthesia usually follows conventional guidelines. Infusions of drugs rather than bolus dosing are preferred, as this achieves smooth uninterrupted anesthesia with good blood pressure control and a high degree of muscle relaxation. The number of pharmacological agents available to the anesthetist is increasing rapidly but we will provide a brief overview of some of these. Propofol is commonly used for maintenance anesthesia and facilitates the reduction of nausea in the postoperative period.[6] Ondansetron, a 5HT-3 receptor antagonist, is a popular antiemetic used in the treatment of postoperative nausea. Ondansetron has equal efficacy to cyclizine or droperidol without the systemic side effects. When given at the end of surgery it has a greater antiemetic effect compared with preinduction dosing.[7] Remifentanil, a new ultrashort-acting opioid drug is ideal for superb levels of analgesia as it is rapidly hydrolyzed by circulating and tissue non-specific esterases. A major advantage of remifentanil is that doses sufficient to attenuate cardiovascular responses can be used without the risk of postoperative respiratory depression. Atracurium is our neuromuscular blocking agent of choice and is infused to achieve tight and flexible control of muscle relaxation during the case. Alternative agents are rocuronium or vecuronium, which are both non-depolarizing competitive neuromuscular blocking agents. Oxygen is administered in air rather than nitrous oxide, which we find unnecessary and likely to cause nausea and bowel distention during the prolonged procedure. Diemunsch et al have demonstrated that nitrous oxide diffuses into a carbon dioxide pneumoperitoneum up to a level that can support combustion in a 2-hour interval.[8] Whether nitrous oxide represents a real clinical risk of fire and explosion is unclear but it is probably best avoided. Inhalational agents are an alternative to the total intravenous technique and the authors favor desflurane because of the fast onset and offset characteristics of this agent. A suitable alternative would be sevoflurane, another modern inhalational volatile anesthetic agent. One useful monitoring practice is the auditory evoked potential or Bispectral Index monitor to titrate the volatile anesthetic: this leads to significant reductions in the anesthetic requirement, resulting in a shorter postanesthesia care unit stay and an improved quality of stay from the patient's perspective.[9]

INTRAOPERATIVE MONITORING

Access to the patient during robotic surgery is poor and generally requires time-consuming de-docking for any serious problems. This is compounded by the necessary use of low light levels for laparoscopic procedures. Good cooperation with the theater team is essential. The monitoring equipment should be checked and working correctly before commencing surgery. Minimal monitoring standards should include temperature probe, electrocardiogram, capnography, non-invasive blood pressure monitoring, and oxygen saturation. Although the authors favor the use of a central venous catheter for monitoring, fluid balance, and vascular access, it is not considered essential in all cases. Indeed, central venous pressure monitoring has very little role in the intraoperative management of patients undergoing laparoscopic surgery, as values tend to be grossly elevated with minimal relation to the patient condition. This is because of the raised intra-abdominal pressures and head-down position. Invasive direct arterial monitoring has a role in the management of patients with significant cardiorespiratory disease but is not generally required. A simple non-invasive monitoring technique of value is Doppler esophageal cardiac output. This measures the velocity of red blood cells in the descending aorta and derives cardiac output and intravascular volume status. This guides fluid therapy intraoperatively, which is very different from an open radical prostate operation where one needs considerably more filling in view of the open abdomen and blood loss.

FLUID REPLACEMENT

Fluid replacement during a robotic radical prostatectomy is not complex in the routine case. Insensible losses are minimal because there are no open wounds and the bowel remains protected and hydrated. Urine output should not be excessive during the dissection phase as the urine will leak from the open bladder and potentially compromise the surgical field. The authors typically infuse 1 L of crystalloid intravenously up to the time of the anastomosis of the bladder neck to the urethra (post removal of prostate) and this is followed by another 1 L of fluid to encourage diuresis towards the end of the case and into the postoperative period. Fluid replacement is judged by clinical response and cardiovascular parameters rather than central venous pressure (see above).

Mean blood losses are usually small in laparoscopic surgery (perhaps only 100 ml measured loss) and therefore maintenance infusion of crystalloid fluid is usually sufficient. Blood transfusion rates with LP or RALP are usually expected to be low at 2–7% requiring transfusion in the perioperative period. The authors withhold transfusion to a level of around 8 g/L in a fit patient. This contrasts with the figures for open radical prostatectomy where the blood loss is typically much more and often over 1 L per case.

GAS INSUFFLATION AND THE PNEUMOPERITONEUM

Both LP and RALP require the formation of a relatively large working space in the pelvis. This is created by the insufflation of between 2.5 and 5.0 L of carbon dioxide gas and subsequent formation of a pneumoperitoneum. The increased intra-abdominal pressure (IAP) used for this type of surgery is an advantage for hemostasis, preventing venous ooze. However, the increased pressure creates a number of potential difficulties:

1. Pneumoperitoneum causes cephalad displacement of the diaphragm, resulting in decreased lung volumes, including functional residual capacity (FRC), decreased pulmonary compliance, increased resistance, and ventilation–perfusion mismatch.[10] Furthermore, the diaphragmatic shift compresses the lungs still further, favoring compression atelectasis.[11] Higher IAP reduces the thoracic compliance and can cause pneumothorax and pneumomediastinum, owing to the increase in alveolar pressures. Patients with extensive pulmonary disease are particularly at risk of complications.[12] Despite the increasing number of LPs and RALPs, there are few clinical trials dealing with the effect of maintaining a prolonged pneumoperitoneum.[13,14] One recent study showed that a positive end-expiratory pressure (PEEP) of 5 cmH_2O improves arterial oxygenation by increasing FRC and tidal ventilation above the closing capacity.[15] This takes place with no apparent effect on hemodynamic variables.
2. Further concern with a high IAP is the potential effect on hemodynamic parameters. Evidence shows that keeping the IAP below 18 mmHg results in only minor changes to hemodynamic variables.[16–19] The increase in IAP results in increased intrathoracic pressure and vascular resistance, causing increased pulmonary and systemic vascular resistances, increased arterial pressures, and decreased cardiac output.
3. Carbon dioxide is the most commonly used insufflation gas during laparoscopy. This is because it approaches the ideal insufflating gas: namely, it is noncombustible, highly soluble, and rapidly excreted. This allows any residual CO_2 pneumoperitoneum to be cleared more readily than with other gases, minimizing the duration of postoperative discomfort.[20] However, CO_2 is not without side effects related to the widespread absorption from the peritoneum, which causes hypercarbia, acidosis, and embolization.[21] This can be a real problem during the initial learning curve of

laparoscopic and robotic surgery when IAPs can be quite high over prolonged periods. Carbon dioxide absorption appears to be greater during extraperitoneal than intraperitoneal surgery and is not influenced by the duration of intraperitoneal insufflation.[22] Not all studies agree with this finding.[16] When the patient is monitored and ventilated under control, hyperventilation may prevent hypercarbia.

4. Other documented effects of pneumoperitoneum include a reduction in splanchnic and renal blood flow and effects on circulating hormones. Plasma concentrations of catecholamines, cortisol, prolactin, growth hormone, and glucose are also noted to be increased.[16–19]

Recent studies recommend a moderate to low IAP (<12 mmHg) as it limits the alteration in splanchnic perfusion, and consecutive organ dysfunctions will be minimal, transient, and will not influence the outcome.[23] Zuckerman and Heneghan[24] demonstrated that these changes are short-lived and lose their statistical significance at 10 minutes from the time the patient undergoes the pneumoperitoneum.

TRENDELENBURG TILT

Trendelenburg or head-down positioning is essential for adequate visualization of the prostate. During RALP this tilt may be as great as 45 degrees. Unsurprisingly, this has an effect both on respiratory and cardiovascular function. When an extreme Trendelenburg position is applied, the central venous pressure increases, and systemic arterial pressures and cardiac output decrease. The effect on the respiratory system depends on the patient's age, weight, pulmonary function, degree of Trendelenburg positioning, anesthetic agents, and ventilation technique. Ventilation–perfusion disparity can result in decreased arterial partial oxygen saturation. General anesthesia, neuromuscular blockade, endotracheal intubation, and controlled ventilation can help to reduce the pulmonary effects of the Trendelenburg position. Both pnuemoperitoneum and Trendelenburg position reduce femoral venous flow, increasing the risk of thromboembolic complications.

This position can lead to a further reduction in FRC. The combined effect of gas insufflation with Trendelenburg position may reduce the FRC below closing volume, which predisposes to airway closure and atelectasis. A decrease in arterial oxygenation and an increase in the ratio of dead space to tidal volume have been demonstrated by Nishio et al in patients undergoing laparoscopy.[25] We have found from our own experience with RALP that the degree of tilt can be lessened as greater experience is gained. We initially started with a 45 degree head down and are now quite capable of managing to operate with a 20 degree tilt. This has obvious benefits for the patient without compromising the ability to perform the procedure. Prolonged head-down positioning does occasionally result in significant edema in the head and neck, but this has not been reported to result in any difficulties in extubation. In fact this edema has resolved spontaneously within the first few hours after surgery.

PERIOPERATIVE ANALGESIA

Radical prostatectomy is a procedure characterized by only moderate pain and a short hospital stay. Whereas the majority of radical prostatectomies are performed under general anesthesia (GA) a number of alternatives/adjuncts are available to provide perioperative pain relief: these include spinal anesthesia (SpA), epidural anesthesia (EA), intravenous opiate infusions, and simple oral analgesia. At present, no consensus has been reached on which modality is best.

Studies have shown that the administration of analgesia prior to a painful stimulus reduces both short-term and long-term requirements for pain relief. Gottschalk et al examined this hypothesis with the use of EA prior to and during RRP. They noted a significant reduction in postoperative pain, including post-hospital discharge pain, following radical prostatectomy.[26] However, detractors of EA point to the 2–5% failure rate and other associated complications including cerebrospinal fluid (CSF) leak, sensorimotor disturbances, and systemic hypotension. Significantly, epidurals may also result in prolonged inpatient stay due to delayed mobilization. Gardner et al confirmed this observation, noting that patients receiving EA combined with GA had longer hospital stays than patients not receiving EA.[27] This obviously has a greater impact in patients undergoing minimally invasive surgery in which early hospital discharge is expected.

Spinal anesthesia involves the intrathecal injection of small doses of bupivacaine with or without opioid; it may offer advantages over epidural anesthesia. SpA is technically easier to perform, allows a faster onset of action, and is also cheaper in cost.[28] The safety of intrathecal opioids has been confirmed by Gwirtz et al, who reported a series of nearly 6000 patients undergoing a variety of operative procedures.[29] The suitability of this procedure during RRP was evaluated by Sved et al, who performed a retrospective study involving 103 patients given a single dose of long-acting morphine. They demonstrated that RRP can be safely performed with SpA, with a mean inpatient hospital stay of only 37.5 hours.[30] Salonia et al found SpA was a credible alternative to GA, with less intraoperative blood loss, less postoperative pain, and a faster recovery.[31] The finding of less intraoperative blood loss with EA or SpA is controversial. Although a number of investigators have confirmed this finding,[32,33] others have not.[34,35]

Whereas we may expect analgesic requirments to be lower for minimally invasive surgery, current evidence does not support this view uniformly. Webster et al studied 314 patients undergoing either RALP or RRP and noted perioperative narcotic use was low regardless of the surgical approach.[36] In fact the modern RRP may have significantly less pain than was previously supposed. Hohwu et al recently showed that RRP may be best treated with simple oral analgesia. This group performed a small randomized prospective study comparing oral oxycodone HCl and paracetamol (acetaminophen) with EA. They found that simple oral analgesia was preferable in terms of analgesic effectiveness and early mobilization as well as cost savings.[37] Despite these findings, the authors' opinion is that intravenous acetaminophen has been a major step forward in the early postoperative analgesic management of these patients. Recent work has also highlighted the importance of intravenous magnesium sulfate in providing an analgesic effect. Magnesium is a physiological blocker of the *N*-methyl-D-aspartate (NMDA) receptors.[38] This might explain the findings of Tauzin-Fin et al, who noted a 50% decreased requirement for tramadol after radical prostatectomy[39] following a bolus injection of 50 ml/kg of magnesium sulfate. Magnesium has also an important role in the postoperative phase for cardiac function, blood pressure and muscle strength, and respiratory impact. Perhaps the best strategy for analgesia involves a multimodal approach providing the benefit of the therapeutic effects of each drug while avoiding the systemic side effects.

POSTOPERATIVE CARE

Following surgery, the decision on the appropriate hospital area for postoperative care will depend on the individual patient requirements. The decision to admit a patient to HDU/ITU (high dependency unit/intensive therapy unit) should be discussed between the anesthetist and the surgeon. The Intensive Care Society

Table 6.1 The Intensive Care UK four levels of care

Level of care	*Patient needs*
0	Patients' needs can be met through normal ward care in an acute hospital
1	Patients at risk of their condition deteriorating, or those recently relocated from higher levels of care whose needs can be met on an acute ward with additional advice and support from the critical care team
2	Patients requiring more detailed observation or intervention, including support for a single failing organ system or postoperative care and those stepping down from higher levels of care
3	Patients requiring advanced respiratory support alone or basic respiratory support, together with support of at least two organ systems. This level includes all complex patients requiring support for multi-organ failure

(UK) has agreed on four levels of care (Table 6.1). The majority of patients will require level 0 or level 1 care but for those with advanced age and significant comorbidities a proportion will require level 2 care.

One of the most important positive predictive variables in radical prostatectomy is the time to return to normal activity. This is important for a number of reasons: early mobilization encourages venous return and helps prevent thromboembolism. Pelvic surgery has been categorized as a high-risk procedure for thromboembolism and a pneumoperitoneum and Trendelenburg position both reduce femoral venous flow. Therefore, the authors routinely give high-dose LMW (low molecular weight) heparin from day 1 postoperatively to avoid thromboembolic complications.

CONCLUSIONS

Minimally invasive techniques are making a major impact on the surgery performed for prostate cancer. This has provided a number of new challenges to both surgeon and anesthetist alike. Whereas the surgeon may have to learn a new set of skills, the anesthetist has to adapt to a new set of physiological conditions imposed on the patient. Although blood loss may no longer be a significant concern, the combination of Trendelenburg tilt and gas insufflation provides a new potential for complications. We have attempted to provide a broad overview of the principles of perioperative care but it has to be remembered that an individually tailored regimen is necessary for each patient. We believe that the role of the anesthetist begins from the preadmission clinic through the perioperative period to the point of discharge. This gives the anesthetist the unique opportunity to optimize fitness and motivate ahead of the surgery. If these points are emphasized, they can in fact be life-changing decisions.

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CHAPTER 7

Lymph node dissection

Fiona C Burkhard, Martin C Schumacher, and Urs E Studer

INTRODUCTION

Lymph node dissection (LND) in prostate cancer remains a controversial issue and, unlike in other cancers, such as colorectal,[1] gynecological,[2] gastric,[3] and bladder cancer,[4,5] its role and importance have yet not been clearly defined. Although it is generally accepted that LND provides important information regarding tumor staging and prognosis (number of nodes involved, tumor volume, capsular perforation), which currently cannot be obtained by other methods, a consensus has yet to be reached as to when an LND is indicated and to what extent it should be performed.

Precise tumor staging is essential to provide an optimal therapeutic management. In patients with prostate cancer the availability of biochemical markers and preoperative biopsies make a differentiated staging possible; however, preoperative lymph node status cannot be determined by these methods. Nomograms and available imaging modalities are also of questionable value. The use of radioisotopes for intraoperative detection of a sentinel node or diseased nodes is time consuming, remains to be standardized, and may have a relatively high false-negative rate. Until reliable detection of micrometastatic disease is possible, templates defining the boundaries of pelvic lymph node dissection (PLND) should be established. This improves staging and allows for identification and removal of minimal metastatic disease. Whether, as with other cancers,[1–5] an additional therapeutic effect of a more extended LND (external iliac vein, obturator fossa, and internal iliac vessels), with removal of all diseased nodes, can be expected, is still not fully determined. This is, at least in part, a result of the relatively benign course of the disease in the majority of patients with prostate cancer.

In this update of the current literature, we review the indications for LND, the extent to which it should be performed, as well as its role in tumor staging and associated potential therapeutic benefits.

PREOPERATIVE ASSESSMENT AND INDICATION FOR PELVIC LYMPH NODE DISSECTION

With the downward stage migration in prostate cancer and ‘lower’ incidence of lymph node metastases that has resulted from aggressive prostate-specific antigen (PSA) screening, it is possible that not all patients require PLND at the time of radical prostatectomy.

However, identifying those patients who would not benefit from PLND remains a challenge.

Patients with clinically localized disease and a PSA <10 ng/ml are considered to be at low risk for metastatic disease and therefore candidates for omission of PLND. However, in our series, 11% of patients in this low-risk group had positive nodes.[6] We found that only patients with a PSA <10 ng/ml and a Gleason score ≤6 in the prostatectomy specimen had a less than 3% chance of lymph node metastasis. However, as approximately 30% of preoperative prostate biopsies are understaged, decision making based on these parameters appears questionable.[7]

Several investigators have developed predictive algorithms, such as the Partin tables and the Memorial Sloan-Kettering Cancer Center Prostate Nomogram, to identify patients at increased risk of lymph node metastasis preoperatively.[8,9] Ross et al catalogued 42 different types of prostate cancer nomograms and concluded that there is a lack of comparative studies on the predictive accuracy of these various nomograms.[10] Moreover, current nomograms have several drawbacks. First, and most importantly, the majority of nomograms are based on results from historical lymph node dissection series without properly defined anatomical boundaries and most of them rely on a limited LND template.[8,9] Secondly, as mentioned previously, a discrepancy exists between Gleason score of the preoperative prostate biopsy and that of the prostatectomy specimen.[7] We found 24% undergrading and 12% overgrading between tru-cut prostate biopsies and the final histopathological results of the prostatectomy specimens.[11] Thirdly, histopathological reporting of the preoperative Gleason score shows a trend towards higher grade assignment since it was first introduced, indicating that the current Gleason score data are not comparable to the data used to establish these different nomograms.[12]

Traditional imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI) are relatively insensitive for the detection of microscopic lymph node metastasis and are often of little help in deciding therapeutic strategies.[13,14] A new imaging modality to potentially detect diseased lymph nodes is high-resolution MRI with magnetic nanoparticles.[15] Although it has been reported that this technique has a higher detection rate than others, it is questionable whether micrometastases can be detected. Multicenter studies demonstrating the reproducibility of this modality are lacking.

Based on these issues, we perform PLND in all patients with a PSA >10 ng/ml and in patients with a PSA <10 ng/ml and a Gleason score ≥6.

INTRAOPERATIVE LYMPH NODE DETECTION

Wawroschek et al introduced sentinel lymph node (SLN) lymphoscintigraphy with gamma probe detection to identify diseased nodes intraoperatively.[16] One disadvantage is that the collimator only detects nodes if it is in close contact (in touch) with the isotope-bearing lymph nodes. Furthermore, nodes are only detected where they are searched for and therefore one cannot be certain that all primary lymphatic landing sites (sentinel nodes) have been identified. Preoperative planar scintigraphy may facilitate the search for isotope-bearing nodes, but has the disadvantage of being less sensitive. Spatial resolution for detection of technetium 99m (Tc 99m)-bearing nodes is improved with three-dimensional (3D) SPECT (single-photon emission computed tomography) and CT or MRI after intraprostatic injection of Tc 99m nanocolloid.

Mattei and associates from our institution applied this method to 34 patients with clinically localized prostate cancer in an attempt to identify the exact anatomical localization of all primary lymphatic landing sites in patients with prostate cancer.[17] Patients with positive

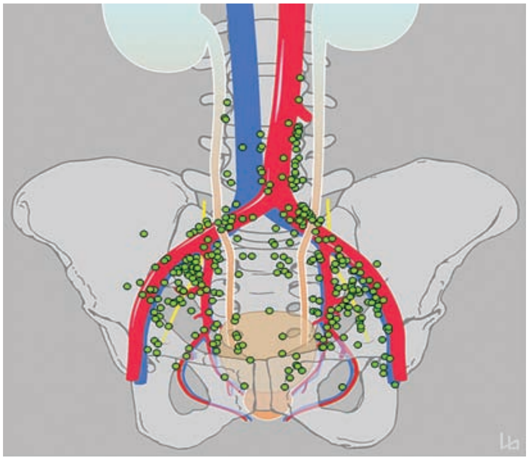

Figure 7.1 Anatomical localization of primary lymphatic landing sites (sentinel nodes) by fusion of SPECT (single-photon emission computed tomography) and CT or MRI in a 3D reconstruction model; this was confirmed by surgical removal. Reprinted from[19] © 2002; with permission from American Urological Association.

nodes were excluded, to rule out the possibility of lymphatics obstructed by cancer cells and so avoid false-negative results. We identified 317 primary lymphatic landing sites in the 34 patients with a median of 10 sentinel nodes per patient (range 3–19). Performing a 3D reconstruction model of the pelvis (Figure 7.1), the primary landing sites were found to be located in the external iliac area in 23%, in the obturator fossa in 17%, along the internal iliac vessels in 17.4%, in the presacral region in 8.2%, in the pararectal region in 3.1%, along the common iliac artery in 18.7%, para-aortal/caval in 12%, and inguinal in 0.6%. The preoperative scanning and the fusion of 3D images as well as the intraoperative search for isotope-bearing nodes by gamma probe was both time consuming and expensive. Intraoperative gamma probe-guided detection of lymph nodes almost doubled the surgical time when compared to an extended PLND. Additionally, if nodal disease is more advanced, the lymphatic tissue may be blocked by tumor cells, resulting in false-negative findings. Gronau et al reported that for this reason in patients with a serum PSA >20 ng/ml a large number of positive nodes (31%) remain undetected by this method.[18] In addition, the 'background signal' generated by the prostate may make detection of potential diseased (isotope-bearing) nodes in the paraprostatic area challenging. Therefore, for the time being a defined template for PLND may be the best approach.

EXTENT OF PELVIC LYMPH NODE DISSECTION

Various templates for PLND in prostate cancer have been described. The most commonly used template is a 'limited' PLND consisting of removal of lymphatic tissue in the area dorsal to and along the external iliac vein and the nodes along the obturator nerve (Figure 7.2). According to the location of primary landing sites determined by Mattei et al, performing a limited PLND in patients with prostate cancer would miss approximately two-thirds of potential primary lymphatic landing sites.[17]

'Extended' lymph node dissection has the following boundaries: cranially, the upper limit of the external iliac vein (leaving the periarteric tissue untouched to avoid lymphedema of the lower extremities, in case later on radiotherapy to the pelvis for a local tumor recurrence is required); distally, the femoral canal (node of Cloquet); proximally, the bifurcation of the common iliac arteries; medially the side wall of the bladder and the obturator fossa and dorsally along the medial and lateral side of the internal iliac (hypogastric) vessels. Lymphatic tissue medial to the internal iliac artery must be included, which some would consider as the presacral/pararectal area (Figure 7.3). With an extended PLND, one-third of potential primary lymphatic landing sites would still be missed according to Mattei et al.[17]

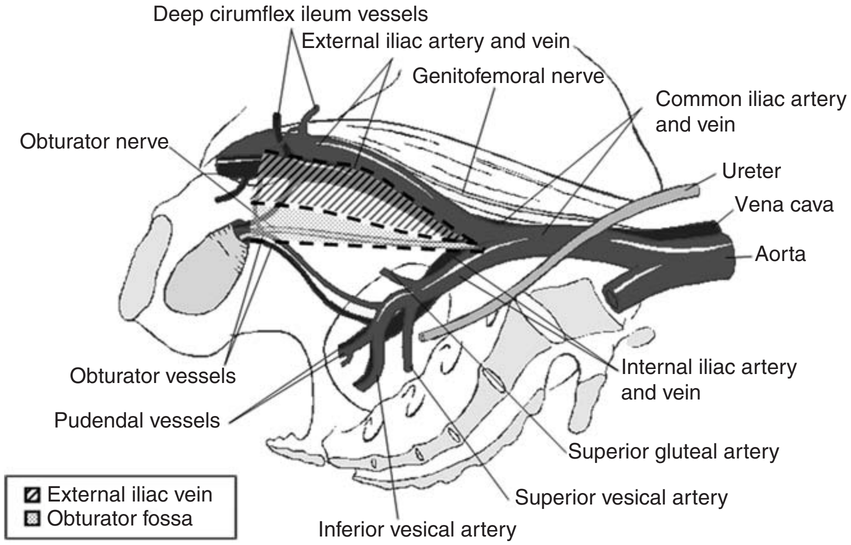

Figure 7.2 Right hemipelvis showing the template of a 'limited' PLND. If lymph nodes are removed in this area, only approximately 25–30% of the primary lymphatic landings sites ('sentinel nodes') are removed.

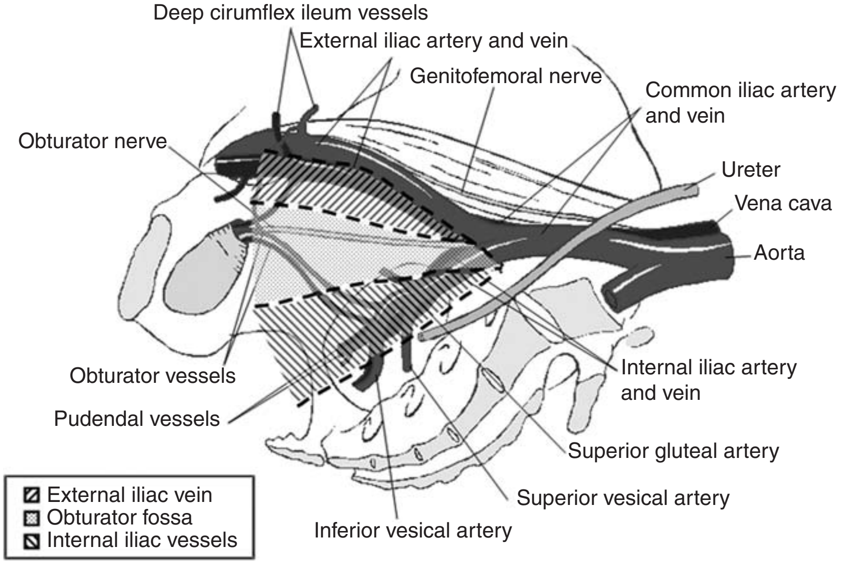

Figure 7.3 Right hemipelvis showing the template of an 'extended' PLND. If lymph nodes are removed in this area, only approximately 60% of the primary lymphatic landings sites ('sentinel nodes') are removed.

Clearly, for accurate staging, LND of all primary lymphatic drainage sites of the diseased organ should be included. However, it is necessary to balance the advantages of removing all primary lymphatic landings sites with the disadvantages of potential morbidity (including damage to vessels and nerves), increased duration of surgery, and associated costs. Based on these concerns, we recommend a 'super-extended' template, similar to that performed for bladder cancer.

In addition to the area of classic extended lymphadenectomy (see Figure 7.3), 'super-extended' lymphadenectomy includes lymphatic tissue along the common iliac vessels up to the crossing of the ureter with the common iliac artery (Figure 7.4). When applying this new template for PLND, an additional 34% (17 of 50 SLNs) of the primary lymphatic landing along the common iliac vessels would be removed.[17] Our personal opinion is that nodes medial to the crossing of the ureters with the common iliac arteries should not be removed, because of the potentially higher intraoperative and postoperative morbidity, i.e. injury to major vessels, lumbar vessels, and the hypogastric nerves.

NUMBER AND LOCATION OF POSITIVE NODES

Before placing patients at an increased risk by performing a more extended dissection, verification that lymph node metastasis corresponds with the identified lymphatic drainage is necessary. By applying a template for an extended PLND, consisting of removal of lymphatic tissue along the external iliac vein, the obturator fossa, and both sides of the internal iliac vessels (see Figure 7.3), a median of 21 (range 6–50) nodes were removed and positive

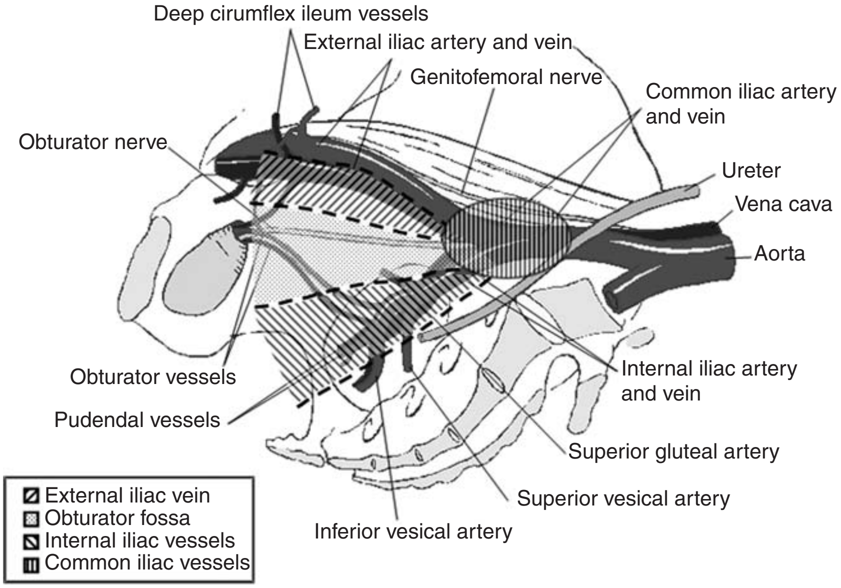

Figure 7.4 Right hemipelvis showing the proposed template for a 'super-extended' lymphadenectomy, which covers the area by classic extended PLND (see Figure 7.3) but includes a larger area along the common iliac vessels extending to the crossing of the ureter with the common iliac artery.

nodes were detected in 24% of patients in our series.[19] The number of nodes removed corresponds well with Weingartner's anatomical study, which determined that approximately 20 removed lymph nodes can be considered a representative pelvic lymphadenectomy.[20] Stone et al compared 150 patients with modified and 39 with extended laparoscopic lymph node dissection; not only did they find, as would be expected, a significant difference in number of nodes removed, 9.3 vs 17.8 (p <0.05), but also diagnosed three times as many patients with positive lymph nodes, 7.3% vs 23.1% ($p = 0.02$).[21] This was confirmed by Heidenreich et al in a comparison of a historical control group with limited (external iliac vein and obturator fossa) and a contemporary group with extended LND (external iliac vein, obturator fossa, internal iliac artery, common iliac vessels, and presacral).[22] A median of 11 (6–19) and 28 (21–46) nodes were removed following limited and extended LND, respectively. At the same time, the number of patients with diseased nodes increased from 12/100 (12%) to 27/103 (26%). These values are significantly higher than the 5–10% positive nodes described in other, albeit not necessarily comparable, contemporary series with limited LND.[23,24] One potential explanation for the noticeably higher percentage of positive nodes detected may be that a significant number of nodes were found outside the standard (limited) area of dissection and thereby the importance of removing nodes along the internal iliac vessels is increasingly evident. Indeed, when performing an extended PLND, almost two-thirds of all patients with positive nodes had at least one positive node along the internal iliac vessels and approximately one-fifth of our patients had them only in this location.[6,19] The proportion of patients with positive nodes either exclusively in this area or in combination with another location was 59% in our series and 67% in a study by Tenaglia and Ianucci.[19,25] Not only would a significant number of patients be understaged if the internal iliac nodes were not removed but also many patients would be left with diseased nodes in place. However, the benefit of a super-extended PLND remains to be shown with prospective studies.

COMPLICATIONS OF PELVIC LYMPH NODE DISSECTION

Opponents of an extended PLND criticize the higher associated morbidity. The typical complications associated with LND are lymphoceles, lymphedema, venous thrombosis, and pulmonary embolism. Reported complication rates for patients with prostate cancer range from 4 to 50%.[26] However, Heidenreich et al found no statistical difference concerning intraoperative complications, postoperative complications, blood loss, and lymphocele formation.[22] In our series of 463 patients, the incidence of prolonged hospitalization or rehospitalization attributable to extended lymph node dissection was as low as 2% and only one patient developed persisting lymphedema.[11] We ascribe our low complication rate to a meticulous surgical technique:

- Ligation, as opposed to clipping of all afferent and efferent lymphatics from the lower extremities. Hemoclips have a tendency to be torn away during the subsequent prostatectomy.
- Placement of two drains instead of one, each draining one side of the pelvis. These drains are not removed until the daily amount drained is less than 50 ml.
- Injection of low molecular weight heparin into the upper arm instead of the thigh.[27]

ADVANTAGES OF PELVIC LYMPH NODE DISSECTIONS

An estimated 20–40% of patients experience a biochemical recurrence (BCR) within 10 years after radical prostatectomy and only one-third of these patients progress from BCR to clinically evident disease. Secin et al reported their results in 387 patients with seminal vesical invasion (SVI) undergoing radical prostatectomy.[28] Of these 387 patients, 91 (24%) had lymph node metastases. A total of 210 patients experienced BCR. For patients with node-negative disease, the 10-year and 15-year freedom from BCR rates were 36% and 32%, respectively, and the corresponding cancer-specific survival rates were 89% and 81%, respectively. For the 91 men who had SVI and positive nodes, the 10-year BCR-free probability was only 10%, but the 10-year cancer-specific survival probability was 74%.[28] Therefore, the interpretation of biochemical failure remains controversial and may not have an impact on survival in the majority of patients.

Lymph node metastasis, however, does have a negative impact on prognosis. In patients with proven node-positive disease, 10-year recurrence/metastasis free rates (without immediate hormonal therapy) range from 10 to 68%[29–35] and cancer-specific survival rates from 60 to 70% (Table 7.1)[30,32,34,36–38] in earlier series with incomplete PLND. This makes persistent disease likely and prognosis is poor. For this reason it is often stated that once patients have node-positive disease, it should be considered systemic disease, and treated accordingly, and further removal of nodes would not benefit such patients. However, there is also increasing evidence that in certain patients surgical treatment with removal of diseased nodes can be curative or at least substantially delay a biochemical relapse. Catalona et al reported on a small series of 12 patients with minimal lymph node involvement (micrometastasis and only one positive node). Without adjuvant therapy, 75% and 58% of these patients remained clinically metastases-free at 5 and 10 years, respectively.[36] In Pound's series for patients with lymph node micrometastases and no adjuvant therapy, the 10-year metastasis-free survival rate was 68%.[37] After a follow-up of 60 and 80 months, 83% and 68% were free of detectable tumor, respectively, in Steinberg's series of 64 patients.[32] In our

Table 7.1 Survival rates in patients with prostate cancer and lymph node metastasis without immediate hormonal therapy

Author	*Number of patients*	*Median follow-up period (years)*	*Treatment (radical retropubic prostatectomy, RRP)*	*Metastasis-free survival*		*Cancer-specific survival*	
				5 years	*10 years*	*5 years*	*10 years*
Han, Walsh[29]	135	6.3	RRP	26%[a]	10%[a]	–	–
Bader, Studer[30]	92	3.75	RRP	~50%	~25%	74%	~62%
Steinberg, Walsh[32]	64	3.75	RRP	83%	68%	97%	62%
Catalona[36]	12	≥ 7	RRP	75%	58%[b]	–	–
Cadeddu, Walsh[45]	19[c]	5.5	RRP	–	–	93%	56%
Messing[46]	51	10	RRP	–	–	–	57%

[a] Recurrence free.

[b] 7 years.

[c] 33% with hormonal therapy, 3% with radiation therapy.

series by Bader et al, 75% of patients with only one positive node remained free of tumor progression and only 14% had died at the time of analysis.[39] Daneshmand et al observed a clinical recurrence-free survival rate of 70% and 73% in patients with one or two positive nodes vs 49% in those with more than five positive nodes.[40] In Steinberg's study the number of positive nodes did not have a significant prognostic value.[32] However, in Frazier's series, two or less positive nodes showed improved cancer-specific survival compared with patients with more than two positive nodes.[41] In our series of 92 patients with lymph node metastasis, time to progression significantly correlated with the number of positive nodes removed.[30] Allaf et al reported a survival difference in men with less than 15% positive lymph nodes; the 5-year biochemical recurrence-free survival rate was 43% vs 10% for extended vs limited lymph node dissection, respectively.[42]

Using the SEER (Surveillance, Epidemiology, and End Results) program database from 1988 to 1991, Joslyn and Konety addressed the question whether a more extended LND and radical prostatectomy resulted in a decreased risk of prostate cancer-specific death at 10 years.[43] According to their results, patients undergoing removal of at least four lymph nodes (node-negative and node-positive patients) or more than 10 nodes (only node-negative patients) had a lower risk of prostate cancer-specific death at 10 years than patients who had no lymphadenectomy. They concluded that a more extensive PLND in patients undergoing radical prostatectomy results in a reduced risk of prostate cancer-specific death in the long term.[43] Similarly, Di Blasio et al showed that the number of nodes removed is associated with progression, thereby supporting a need for extended PLND.[44] Removal of 13 nodes had the lowest risk of disease progression, regardless of nodal disease status in their cohort of patients. Bader et al reported similar findings, with 16%, 12%, 8%, and 8% of patients showing disease progression after removing 0–4, 5–9, 10–14, and >14 nodes for pT1/pT2N0 prostate cancer, respectively.[39]

There are few reports addressing the ratio of positive nodes in prostate cancer. In a series from the Johns Hopkins Institution, 52% of patients with less than 15% positive nodes, Gleason score below 7, and negative seminal vesicle invasion remained free of progression at 5 years.[40] Similarly, Daneshmand et al reported that patients with a lymph node density (percentage positive nodes/total removed nodes) of ≥20% were at a higher risk for progression than those with a density of <20%.[40]

Overall, there is increasing evidence indicating that some patients with minimal lymph node metastasis (less than two positive nodes, low metastatic volume) do have a good chance of asymptomatic long-term survival, if all diseased nodes are removed. If all primary landing sites, as determined by Mattei and coworkers,[17] are included in a template, minimal metastatic disease which would otherwise remain undetected would be removed. This may partly explain the prolonged survival observed with removal of more nodes, even if they are presumed negative.

CONCLUSIONS

Preoperative assessment does not adequately predict lymph node metastasis. An increasing body of evidence suggests that PLND should be performed in all patients with a PSA >10 ng/ml. In patients with a PSA ≤10 ng/ml, PLND is only indicated if the Gleason score is ≥7. If PLND is performed, we now advocate a 'super-extended' PLND based on information regarding the multiple primary landing sites of the prostate. There is an increasing amount of data suggesting that an extended PLND in prostate cancer not only improves the accuracy of tumor staging but also that complete removal of metastatic disease provides a therapeutic benefit in patients with micrometastases to only a few nodes.

Morbidity of LND can be kept minimal if the lymphatics draining the lower extremity are ligated as they enter the pelvis.

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Part 3: Open radical prostatectomy

CHAPTER 8

The anatomical radical retropubic prostatectomy step by step

Robert P Myers

> Your fingers are your best instruments; use them!
>
> Ormond S Culp

INTRODUCTION

For clinically localized prostate cancer, many surgical approaches to radical removal of the prostate have been described. Patients want a 'clean sweep' of their cancer, but afterward they want decent quality-of-life outcomes. This chapter describes one current meticulous technique as evolved after more than 30 years and more than 4350 consecutive open radical prostatectomies. This open technique involves a balance in the use of hands and instruments to remove prostate, seminal vesicles, and regional lymph nodes. The reader should, with the illustrations provided, be able to comprehend exactly how to accomplish this technique. In a surgical atlas approach, the operation is described in progressive subsections in the imperative in **Steps** with prefatory principles and parenthetical commentary where germane. Nuances and potential pitfalls are included in accompanying **Notes** and **Warnings**. All key steps from beginning to end are explained. If the operation is done properly, given appropriate selection of patients, a skilled surgeon should expect consistently good results. Goals include oncological safety (negative margins of resection), preservation of urinary control (at least pad-free and no bother), and recovery of erectile function (satisfactory intercourse). Introduced with the concept of preserving erectile function,[1] preservation of the neurovascular bundle (NVB) may also have a role in the return of urinary control.[2] Patients in the radical prostatectomy age group may report some erectile dysfunction preoperatively. *No surgeon in the world can ever guarantee functional outcomes – a message that should be made clear to every patient as part of the informed consent process.*

The operation described herein involves a disciplined team approach with key members, appropriate operating room conditions, and skilled communication (Appendix A). The goal is removal of prostate, seminal vesicles, and regional lymph nodes while exacting minimal tissue injury to the structures to be preserved, in particular the NVBs, membranous urethra with its striated urethral sphincter, and the levator ani as major elements of pelvic floor protection.

INSTRUMENTS

Having all the right tools obviously facilitates the operation. Laparoscopists have shown that *magnification provides substantial advantage in viewing and defining fine anatomical structure*. In open surgery, a comparable field of view is obtained at nominal cost with prescription glasses having 4.3–4.5 power through-the-lens telescopes tilting 20° downward and lenses mounted in a titanium frame for lightness (Figure 8.1). To obtain the very best technical results with minimal blood loss, 4.3–4.5 power is strongly recommended throughout the operation ('skin-to-skin'). At less than 4.3 power, it may not be possible either to view adequately the very fine anatomy involved or to conduct proficiently each step as described herein.

In addition to four surgical field lights directed into the recesses of the abdominal opening, a forehead, centrally placed headlight with xenon light source adds to illumination. Most of the special instruments used are detailed in Appendix B. Hemostasis depends primarily on 3-, 6-, 8-, and 10-mm titanium clips and 5-0 poliglecaprone and 3-0 polyglactin suture on fine-caliber needles. During surgery, routine double-gloving minimizes risk of 'sharps' injury and also exposure to hepatitis and human immunodeficiency virus in a patient's blood. For the hand of an average-sized male surgeon, size No. 8 gloves covered by size No. 7½ gloves serve the purpose without causing significant loss of tactile sensation. For hemostasis well removed from the NVBs, some fascial incisions, and portions of the bladder neck resection, monopolar electrocautery is used at variable settings. Two wall-suction devices are consistently available, consisting of one plastic Yankauer and one metal suction tube (Andrews-Pynchon) or two of the metal suction tubes with drainage holes very close to their ends for the driest possible field of vision at the time of the critical prostate apical dissection.

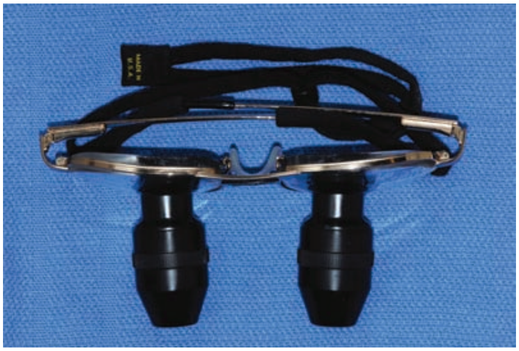

Figure 8.1 Optical loupes of 4.3 power.

ANESTHESIA, ANALGESIA, AND MEDICATIONS

For rapid cognitive recovery, the postoperative use of opiates is assiduously avoided, and the duration of hospitalization is minimized (preferably to no more than one night) by using a program of preemptive analgesia. This program currently includes preoperative administration of oral celecoxib 400 mg and gabapentin 600 mg in the patient holding area. In the operating room, midazolam up to 2 mg and fentanyl up to 100 μg are used for sedation, and an L3–4 interspace single-shot spinal anesthetic is administered using a combination of 2 ml of bupivacaine 0.75% plus hydromorphone 0.04 mg and clonidine 0.04 mg. General anesthesia is induced with administration of propofol up to 150 mg. Cisatracurium up to 10 mg or succinylcholine up to 120 mg is used to facilitate airway intubation, and a light general anesthetic (oxygen, nitrous oxide, sevoflurane or isoflurane) is administered. For local effect, the skin incision is marked in purple, and the epidermis and dermis are then infiltrated with a 2% lidocaine–0.5% bupivacaine mixture in a 1:4 ratio. Dexamethasone 8 mg is given to prevent pruritus, and ondansetron 4 mg is given as an antiemetic. At the end of the operation, intramuscular ketorolac 30 mg intramuscularly is given with 30 mg subsequently provided every 6 hours for no more than 48 hours. The ketorolac administration is alternated with extra-strength acetaminophen 1 g every 6 hours with a 3-hour offset for the two medications. For patients 65 years or older or with a serum creatinine value of 1.5 mg/dl or more, the dose of ketorolac is halved. This program permits next-day discharge for approximately 70% of patients. On discharge, prescribed analgesia includes extra-strength acetaminophen 2 pills every 6 hours as needed with a backup regimen of more potent propoxyphene napsylate 100 mg with acetaminophen 650 mg or tramadol 20 mg on a similar schedule.

During dissection, if a hypercoagulable state evidenced by any pelvic vein thrombosis is noted, sodium heparin 5000 U is given immediately subcutaneously over the deltoid muscle as prophylaxis against further thrombosis. All patients in bed after surgery lie in modified semi-Fowler position with back flat and legs elevated 30° with heels higher than the heart, and a program of active foot dorsiflexion against a footboard is instituted.

Oral milk of magnesia 4 oz is prescribed for the evening of the day of discharge, and if an appropriate response is not forthcoming the next morning, a 6- to 8-oz bottle of oral citrate of magnesia at noon is recommended.

PATIENT PREPARATION

The day before surgery the patient is instructed to eat a soft diet with nothing solid after midnight. Clear liquids are acceptable up to 2 hours before anesthesia. The evening before surgery, the patient is recommended to shower with chlorhexidine or povidone-iodine soap application from the neck down and ordinary shampoo for the head and neck region. Before the shower, the patient is instructed to self-administer and complete the elimination of two phosphosoda enemas. On admission to the hospital, two additional similar enemas are provided. Combined antibiotic and mechanical bowel preparation is reserved for patients at high risk for rectal entry; for example, those with seven previous transrectal needle biopsies or multiple saturation biopsies through the rectal wall. [**Note**: Surgeons who are new at radical prostatectomy may want to consider a combined antibiotic and mechanical bowel preparation for all patients until they are comfortable with their technique.]

POSITION ON OPERATING ROOM TABLE

For both pelvic exploration and reduction of airway ventilation risks, optimal patient position is maintained. For most patients, the position is supine with slight flexion at the waist (1) to tilt the pelvis toward the feet to improve access to the prostate and (2) to increase the sternum-to-pubis distance, thereby flattening the abdomen with a commensurate decrease in the anteroposterior distance at the umbilicus. Excessive flexion should be avoided because it may lead to lumbosacral pain in the postoperative period, notably in patients with lower back degenerative arthritis or subclinical spinal stenosis. Furthermore, excessive flexion may produce femoral nerve stretch, which might cause temporary leg weakness, loss of knee reflex, or meralgia paresthetica. On the basis of the history, some patients may need to be perfectly flat during the entire operation. Temporary reverse Trendelenburg position aids the apical dissection, and temporary Trendelenburg position assists the seminal vesicle dissection. Otherwise, the abdomen is kept essentially parallel to the operating room floor during surgery.

With electric clippers, the patient is shaved from nipple to mid thigh, including the perineum. The skin is scrubbed and then painted with povidone-iodine soap and paint, respectively. The abdomen is draped in preparation for a low midline abdominal incision, and a sterile 20-Ch silicone-coated urethral catheter is introduced into the urinary bladder and its balloon inflated to 20 ml.

INCISION

Open radical retropubic prostatectomy does not work without adequate access to the prostate. For a standardized extraperitoneal approach, a universally applicable 20-cm incision is described. *The smaller the incision, the less tactile discrimination is possible*. The incision should be large enough to provide workable exposure for all patients regardless of body habitus, including variably sized or configured pelves. The prostate may be very accessible in some patients or very inaccessible in others; that is, the pelvis varies from broad and shallow with a wide pubic arch (more gynecoid) to narrow and deep with a narrow pubic arch (more android). Therefore, for optimal utility, the lower midline abdominal incision is recommended to extend from symphysis to umbilicus, skirting to the left and above the umbilicus for about 1 cm. The skin incision should not be carried too close to the penis in order to prevent postoperative penile and scrotal edema.

The 20-cm incision allows an extraperitoneal opening large enough (1) for optimal Balfour retractor (Balfour) retraction, (2) to be sufficient for extended bilateral pelvic lymphadenectomy when indicated, (3) to admit simultaneously the tips of each index finger to palpate the prostate and position of the catheter with respect to the apex of the prostate and prostatourethral junction, and (4) to allow enough room for a single hand to grasp the entire prostate during dissection while permitting each index finger to guide NVB preservation. Thus, by finger palpation, prostate size and apical prostate configuration should be judged, including length of the anterior commissure or distance from the bladder neck to the prostatourethral junction. Also assessed is how much benign prostatic hyperplasia (BPH) is present forming the anterior commissure and how BPH, if present, is disposed relative to the prostatourethral junction. The extent of BPH affects how control of the dorsal vein complex (DVC) will be facilitated and how many progressive sutures will be used close to the midline in the distal bunching of the DVC, as described below. Additionally, during manual palpation and tactile discrimination, areas of cancer induration or nodularity should be appreciated for avoidance during dissection.

Steps: 1. First draw the skin incision line with a sterile marking pen and, along the line, infiltrate the epidermis and dermis with the lidocaine–bupivacaine mixture mentioned above. (With incision 20-cm long, and lateral and central Balfour blades placed correctly, the retropubic extraperitoneal access should be, distal to the midline Balfour blade, a working diamond-shaped cavity about 5-in [12.5-cm] wide, 4-in [10-cm] long after retracting the peritoneum and bladder, and 2- to 5-in [5- to 12.5-cm] deep depending on the shape of the patient's pelvis.) [**Note**: From umbilicus to pubis, the less subcutaneous adipose tissue there is, the better. An active weight-reduction program with diet and exercise in the weeks before surgery is encouraged.] **2**. Once the skin and subcutaneous incision have been developed, incise the anterior rectus abdominis (rectus) fascia in the midline from the pubis to a point midway between the umbilicus and the inferior margin of the posterior rectus fascia. Now incise the fascia laterally for 1 cm either to the left or to the right of the midline over one rectus belly. From that point carry the fascial incision superiorly in the fascia parallel to the subjacent rectus fibers to a point just superior and lateral to the umbilicus. (This maneuver provides a 1-cm flap of fascia along the upper aspect of the incised rectus fascia to make the closure easier and stronger.) **3**. Now, in the midline, incise the transversalis fascia. **4**. Laterally identify, cross-clip, and divide each vas deferens.

5. For placement of the blades of the Balfour, bluntly develop and enlarge spaces above each iliopsoas muscle. **6**. Place rolled lap sponges over the edges of the incision and into the spaces to protect the wound edges from the Balfour blades. **7**. Place the lateral Balfour blades and initiate lateral retraction of the padded wound edges. **8**. While digitally holding the posterior rectus fascia upward on tension, use a No. 10 scalpel blade held at 45° to score and divide the inferior posterior rectus fascia for 3–4 cm, taking care not to enter the peritoneal cavity. **9**. Retract further the blades of the Balfour. (For full retraction it may be necessary to incise the anterior rectus fascia further cephalad and further distally above the symphysis. In general, for patients of short stature, it will be necessary to work through a smaller aperture than for taller patients, and therefore full retraction of the Balfour blades will not be possible. The size of the central Balfour blade should be selected accordingly.) **10**. Once the wound is fully retracted laterally, insert a central blade, deep and broad enough, to hold peritoneal contents and bladder down and backward with the Foley balloon caught under and cephalad to the leading edge of the retractor blade. (This must be done in a way that the NVBs are never placed on tension.) [**Note**: The Balfour is a very unobtrusive retractor for this operation because it is positioned at skin level and therefore allows optimal use of hands and fingers deep within the wound with the skin incision as described above. The central blade should never be placed in such a way that the NVBs are placed on stretch and thereby injured. Ring retractors, such as the Buchwalter, may impede manual dexterity. **Warning**: Excessive lateral tension on the Balfour blades may tear the rectus. The blades should be opened gently. Too much tension on the rectus also may press the lateral femoral cutaneous nerves as they exit from the lateral inguinal canal, causing meralgia paresthetica in the postoperative period. Also, the blades must not impinge on the iliac vessels or femoral nerves.] **11**. Desiccate with electrocautery or manually push aside loose, cotton-candy-like, pelvic areolar fascia to develop perivesical spaces for bilateral pelvic lymphadenectomy. **12**. Use Singley forceps to remove all visually obstructive adipose tissue (fat) in the retropubic space. If present in the midline, identify, ligate with 3-0 silk, or cauterize, depending on diameter, the superficial vein from the DVC (approximately 80% of cases[3]). During the process of fat removal, identify the presence or absence of supralevator accessory or aberrant pudendal arteries and determine the possibility of saving them. Remember that in some cases penile blood supply is exclusively supralevator, and the classic infralevator blood supply through Alcock's canals does not exist.[4]

BILATERAL PELVIC LYMPHADENECTOMY

Lymph nodes are routinely removed as a package from the obturator fossa bilaterally and, when indicated, extended to include the sentinel external iliac lymph nodes.[5] An extended dissection is reasonable in the presence of high-grade or high-volume prostate cancer. Finding a positive or tumor-bearing lymph node is not taken as an indication to abandon removal of the prostate as long as the patient can look forward to a decent functional outcome. When every milliliter of cancer is said to contain 10^8–10^9 cancer cells depending on the grade of malignancy,[6] the aim is to remove as much cancer as possible. The timing of adjuvant hormonal therapy may be considered in the postoperative period, depending on serum prostate-specific antigen level (PSA) over time.

Before beginning the node dissection, place the Dixon malleable center blade on the Balfour to retract the bladder medially away from the obturator fossa. To enlarge the operative field when necessary, ask the second assistant to retract the bladder further medially with a long Harrington retractor.

Steps: **1**. For limited dissection, begin by isolating, with 3- and 6-mm titanium clips, lymphatics first along the surface of the external iliac vein and proceed posteriorly around its circumference until the obturator internus muscle is identified on the lateral aspect of the obturator fossa. **2**. Look for venous branches that emanate posteriorly from the external iliac vein, and control these branches. **3**. Identify and clip any tiny arteries that pierce the obturator internus muscle and enter the node package. **4**. Identify the obturator nerve throughout its course along the obturator fossa so that it is plainly in view at all times and therefore not subject to inadvertent injury. If the obturator nerve is ever injured, repair it with multiple interrupted sutures of 7-0 polypropylene and cover the repair site with fibrin glue. **5**. With an index finger, free medially the obturator nodes from the obturator muscle in a bundle above the obturator nerve. **6**. Cross-clamp with a single Shallcross forceps (Shallcross), transect, and ligate with a 2-0 silk tie the distal end of the obturator node package. **7**. With the transected end of the node package on upward traction using a Shallcross, free with continued clip application the proximal end of the node package where it approaches the obturator nerve, vein, and artery. **8**. For more extended lymphadenectomy, remove en bloc with the obturator nodes those contiguous internal and external iliac lymph nodes that lie in a group just distal to the bifurcation of the common iliac artery into its external and internal branches. [**Note**: The obturator artery is sometimes a source of unanticipated collateral penile blood supply and should not be injured. Bulldog clamping of the internal iliac artery is not used specifically because of the voluminous collateral superior and inferior gluteal arterial flow distal to the usual point of clamping. The crux of hemostasis rests primarily in control of the DVC, inferior vesical arteries, the main prostate vascular pedicle, arteries that bleed incessantly along the NVB, and bleeding on the surface of the prostate before main prostate vascular pedicle control.]

BEGINNING MOBILIZATION OF THE PROSTATE

Until the endopelvic fascia is opened, the prostate is completely obscured from view by the detrusor apron portion of the anterior bladder wall[7] and associated vesicopudendal venous (Santorini) plexus.

Steps: **1**. After completing the bilateral pelvic lymphadenectomy and obtaining a relatively dry field with full retropubic space development, open the endopelvic fascia bilaterally with the tip of a No. 15 scalpel blade (Figure 8.2A). With the other hand, retract the bladder medially to an extent that the endopelvic fascia is taut and even pulled off underlying levator muscle to create a free space beneath the fascia. **2**. Make the curvilinear line of incision approximately 0.5 cm lateral to the white fascial tendinous arch from the puboprostatic (pubovesical) ligaments to a point just distal to the prostate vascular pedicle, recognizable by large veins that need, at this juncture, to be avoided. (These veins will be managed later when the prostate vascular pedicle is ligated.) **3**. Use curved, pointed scissors to transect anterior to the vascular pedicle the fascial tendinous arch toward the midline while avoiding any underlying veins. (This cut facilitates midline bunching of the DVC over the anterior commissure of the prostate and placement of the proximal bunching suture described below.) **4**. Once the fascia has been appropriately incised, displace laterally, with the tip of the index finger or fine instrument, any remaining levator muscle fibers adherent to and obscuring the lateral surfaces of the prostate. (After bunching, the lateral surfaces of the prostate will blanch with variable numbers of compressed veins coursing from the NVBs to the anterolateral components of the DVC.)

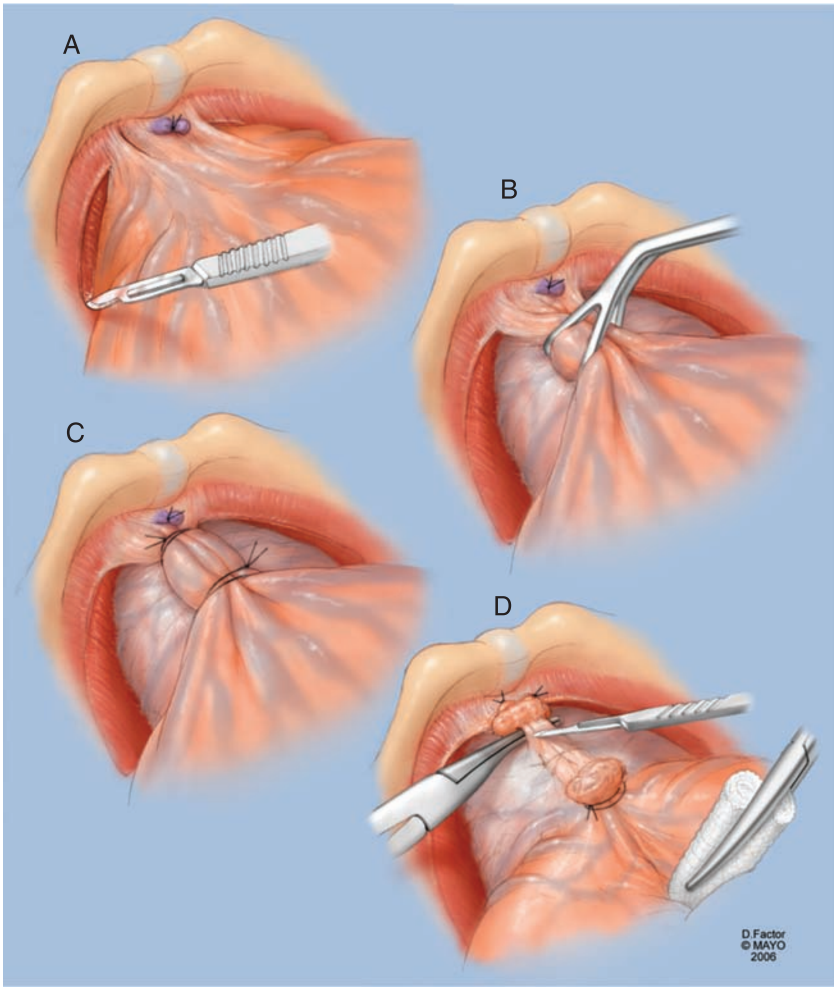

Figure 8.2 Bunching of dorsal vein complex. (A) Endopelvic fascia opened with No. 15 scalpel blade. (B) Forceps in place well removed from neurovascular bundle and prostatourethral junction. (C) Bunched tissue held with sutures and forceps removed. (D) Bunched dorsal vein complex transected between sutures. Final transection distally with No. 15 scalpel blade (technique after that of Walsh[9]). (Used with permission of Mayo Foundation for Medical Education and Research.)

BUNCHING

Control of the DVC involves bundling of the loose tissue spread across the anterior surface of the prostate above its commissure.[8] This tissue is composed primarily of veins, sometimes small arteries, and, toward the midline, the detrusor apron that culminates in pubovesical (officially, puboprostatic) ligaments. If this loose tissue is not brought together as a preliminary maneuver, the prostate will be essentially obscured throughout its removal and orientation will be more difficult. The basic principle is to bunch the tissue together in such a way that the NVBs and striated urethral sphincter are not disturbed. If these precepts are followed, the technique described below should be safe.

Steps: 1. Examine the anterolateral prostate for the edges of the opened endopelvic fascia, which will be grasped by the jaws of the modified Babcock forceps. **2**. With the forceps, compress all the midline loose tissue on the anterolateral surface of the prostate, including veins and detrusor apron, into a tight midline bundle (Figure 8.2B). Always place the forceps at mid anterior commissure proximal to the prostatourethral junction and never over the membranous urethra where it could damage the striated sphincter and NVBs. [**Note**: If the forceps is applied properly, there is no disturbance of the NVBs. Bunching works best when the prostate is of moderate size and anastomotic veins are not plentiful. When the prostate is extraordinarily small, for example, 15 g, the forceps ends are large relative to the size of the prostate. The forceps ends must always engage the anterolateral plexus anterior to the NVB, so as not to grab the NVBs by mistake. Bunching is less effective if the entire sides of the prostate, unilaterally or bilaterally, are covered by veins. More will need to be done hemostatically than just simply bunching to prevent back bleeding. This can be accomplished with figure-of-eight 5-0 poliglecaprone sutures. If the prostate is, for example, greater than 100 g, the plexus and detrusor apron will be attenuated over anterolaterally protruding BPH and it may be difficult to bring the required tissue into the midline with the forceps. In those rare instances of extensive high-grade anterior cancer with invasion either of the detrusor apron and anterior bladder wall more proximally or of the DVC and striated sphincter distally, bunching will be both difficult and ineffective and risk a positive margin. When the tissue will not bunch together easily over the anterior commissure, anterior cancer should be suspected and avoided during the prostate mobilization process by keeping the cancer covered with contiguous fascia or a portion of the decompressed but controlled DVC tissue. For anterior cancer invading the bladder neck, wide bladder neck resection will be necessary, and DVC control across the anterior surface of the prostate is modified with multiple figure-of-eight hemostatic 3-0 polyglactin sutures.]

SUTURING AND TRANSECTING THE BUNCHED TISSUE

When bunching is completed after suture placement, as described below, the edges of the DVC will be hyperbolic in their distribution over the anterolateral prostate. Proximally, the veins will fan out on either side to enter the bladder and internal iliac veins. Distally, the veins will fan out to cover the prostatourethral junction as they course toward the penile vascular hilum and anastomose with veins within each ischioanal fossa laterally and within the pubic arch medially.

Steps: 1. Once the forceps is accurately placed where the prostate is judged to have its greatest girth, pass a suture of 1 polyglactin on a CT taper needle first proximal and then distal to the clamped tissue. **2**. While facing the foot of the table to place the proximal suture and the head of the table for the distal suture, pass the needle tangential to the surface of the prostate without entering prostate. Make each suture a figure-of-eight, the initial pass close to the prostate and the second pass more superficial. **3**. Remove the forceps and the bunched tissue will now be held in the desired midline bundle (Figure 8.2C). [**Note**: An exception is the presence of an accessory or aberrant pudendal artery diving in distally above the prostatourethral junction, in which case the forceps is removed before tying down the distal suture so that the tie will not interfere with and inadvertently occlude the artery by undue external tissue pressure. It is very important to place sutures for venous control posterior to the artery as it enters distally.] **4**. With pointed Metzenbaum scissors (pointed Metz), cut, halfway between the proximal and first distal bunching suture, the bunched tissue transversely to a level just shy of the anterior surface of the prostate. The most posterior layer of the DVC should be left to cover the anterior surface of the prostate to avoid a positive anterior margin. **5**. Turn the pointed Metz with the curved tips upward and develop what is a relatively avascular plane toward (but stop well shy of) the distal bunching suture. **6**. Use the Kittner dissector to push away levator muscle along the fascial boundary of the prostate and membranous urethra or as close to it as possible. (This step is easier if the prostate is relatively small than if there is considerable BPH.) **7**. Palpate with index fingers the position of the catheter within the membranous urethra and judge the distance and amount of tissue from the prostatourethral junction to the distal bunching suture. (This distance will vary depending on the size of the prostate and the presence or absence of BPH.) **8**. Marching progressively toward the prostatourethral junction, continue to use additional distal sutures as needed to secure the DVC. If the prostate is large, pass a second 1 polyglactin on a CT taper needle. If the distance is relatively short and there is little tissue to palpate, use a 1 polyglactin on the smaller CT-2 taper needle. The more BPH is present, the more successive distal bunching sutures will be needed until palpation suggests only a tiny gap remaining between the prostatourethral junction and the most distal suture. [**Note**: Using two sponge sticks, the first assistant will need to apply pressure downward and cephalad at the vesicoprostatic junction while the distal sutures are being placed. When the suture is tied, the first assistant uses only one sponge stick, pressing downward in the midline at the bladder neck. If the retraction is excessive, the distal bunched tissue may slip out away from the first distal suture, causing complete loss of vascular control with extensive venous bleeding. This creates an emergency situation. With severe venous bleeding, sponge-stick retraction should be immediately suspended to induce temporary venous hemostasis until everyone on the team is ready to secure bleeding vessels, which will be accomplished with 5-0 poliglecaprone. Two suction devices and tips should be available and used to allow the bleeding points to be seen and accurately secured. While the first assistant retracts with sponge sticks, the second assistant uses the two suction devices. By facing the head of the table, the open venous ostia are identified and closed with multiple continuous sweeps vertically, first on one side of the sphincter and then the other. Working quickly avoids massive blood loss. Midline venous ostia are similarly closed while staying anterior to the underlying striated urethral sphincter. Sometimes it will be possible to bring all bleeding under control with one suture by gathering tissue continuously in the midline starting at striated sphincter level and progressing anteriorly. With lesser magnification than 4.3 power, individual bleeding venous ostia will be difficult to discriminate, and the reflex reaction under circumstances of pronounced bleeding is to use a larger needle. In so doing, the striated urethral sphincter and the NVBs may be irreparably injured. Any sweep that passes too far distally into the penile hilum may damage dorsal sensory nerves of the penis. With use of a tiny needle, such as the RB-1 taper with 5-0 poliglecaprone, adverse events are much less likely to happen. The goal in suture placement is to stay medial to the NVBs and anterior to the striated urethral sphincter and no more distal than sufficient to close the individually identified open venous ostia.] **9**. Once the most distal bunching suture in the series is secured, pass the tip of an Adson forceps (Adson) through the gap between the most distal bunching suture and the striated urethral sphincter. **10**. Into the opened tip of the Adson, have the first assistant pass the non-needle end of a 0 polyglactin suture with a CT-2 taper needle and pull the suture end through the gap.

11. Now tie this suture to encompass all remaining DVC. **12**. Then pass the needle end of the same suture through the bunched tissue and tie to provide an effective final figure-of-eight suture to encompass all remaining DVC. **13**. Check the anterior surface of the prostate and use 3-0 polyglactin with an SH taper needle in figure-of-eight technique to reinforce proximal bunching or any anterior bleeding tissue. **14**. Place the tip of the Gemini forceps in the aforementioned gap to protect the striated urethral sphincter and to guide the direction of the final sharp cut, initially cutting with pointed Metz and finalizing with a No. 15 scalpel blade down to the Gemini without cutting into prostate tissue (Figure 8.2D). (The prostatourethral junction with visible striated urethral sphincter should come into view. Striated urethral sphincter fibers are red-brown. The first fibers to be seen may appear to run vertically; however, with BPH one may see the striated urethral sphincter as the anterior surface of a smooth cylinder with its distinctive red-brown hue. The red-brown soft sphincter contrasts sharply with the rubbery, white anterior prostate. When there is no BPH, the striated urethral sphincter often fades gradually into the anterior commissure, making the precise junction of sphincter and prostate much more difficult to discern.) [**Warning**: The use of a large angled forceps, such as the Shallcross or the Stille (see Appendix B), for encompassing the DVC and passing the distal bunching suture, carries risk of damage to the striated sphincter and the NVBs, especially when the prostate is small and there is no BPH.]

ANTERIOR URETHRAL TRANSECTION

The principle is to first transect the striated urethral sphincter in its anterior half until the urethral wall smooth muscle is reached and then to cut the urethral wall smooth muscle to expose the catheter.

Steps: 1. At the lateral aspects of the proximal sphincter, look for flanking white bands of fibrous tissue (‘pillar’ tissue[9]) to be clipped with appropriate-sized titanium clips and to be cut to expose the anterior surface of the prostate beneath the bands, which overlie and obscure the underlying NVBs (Figure 8.3A). This tissue represents the thickened edges of the DVC into which the thin anterior layer of the striated urethral sphincter is inserted.[10] These remnant edges or fibrous bands of the DVC may be vascular with venous sinuses. Beginning relatively narrow at the prostatourethral junction and widening distally, the bands vary in thickness and width, and if they are particularly broad it may be necessary to use a transversely applied 6-mm clip distally and a 3-mm clip proximally. **2**. By steadying the tip of an Adson beneath the band close to the prostatourethral junction, flatten the bands to apply clips expeditiously. Apply clips first distally and then proximally. (The proximal cross-clipping should not be exactly at the prostatourethral junction because the bands are a path for direct distal invasion by prostate cancer and a source of an anterolateral positive surgical margin.) **3**. In some cases, the bands are scanty, and only a thin layer of fascia flanks the sphincter. In such cases, with the prostatourethral junction exposed, place 3-mm clips into the fascia approximately 1 and 3 mm distal to the prostatourethral junction. **4**. In each case, with the second assistant retracting the vesicoprostatic junction cephalad with a sponge stick as before, cut with curved scissors or pointed Metz between the proximal and distal clips to a depth that does not infringe on the circumference of the striated urethral sphincter past the 3 o’clock position on one side and the 9 o’clock position on the other. It is important to maintain an intact fascial surface on the posterior half of the sphincter at the prostatourethral junction. **5**. Against this posterior fascia, first on one side and then the other, run the tip of the Adson so that it hugs the outside of the fascia and pass it along the prostatourethral junction

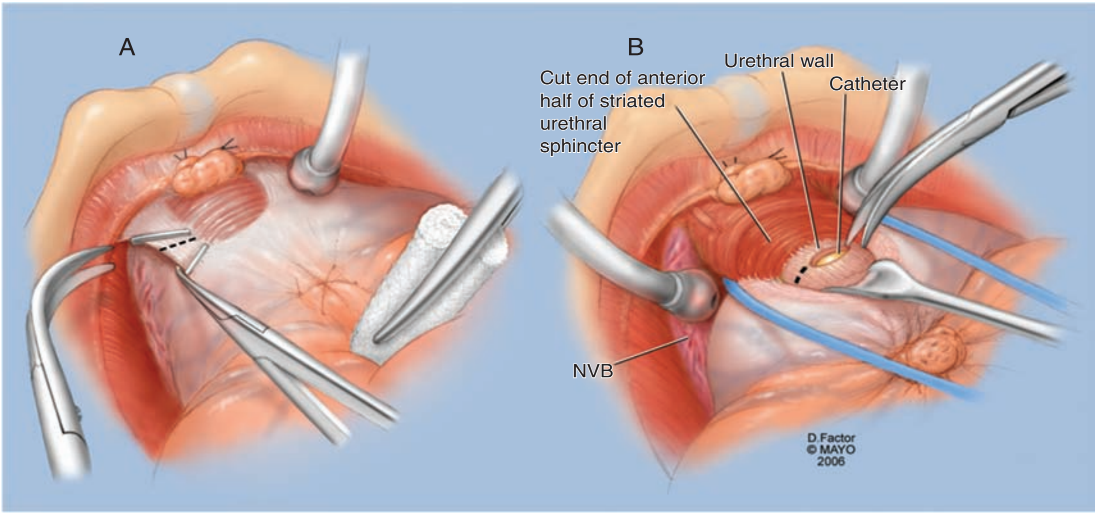

Figure 8.3 Anterior urethral transection. (A) At left of striated urethral sphincter, cross-clipped lateral fascial band about to be transected along dashed line beyond prostatourethral junction. (B) Transection of smooth muscle urethral wall along dashed line 3 mm proximal to already transected anterior half of striated urethral sphincter. NVB, neurovascular bundle. (Used with permission of Mayo Foundation for Medical Education and Research.)

until reaching the posterior fibrous tissue raphe (raphe). During this maneuver, the tip of the Adson should pass medial to the NVBs in the middle of the triangle created by the NVB laterally and the urethra and the prostate medially. [**Warning**: Do not make the mistake of passing the Adson tip between fascia and sphincter, thereby producing injury to the relatively soft sphincter. The initial passage of the Adson tip will generally not be directly posterior but more diagonally downward and caudal, especially if the prostate has an anterior apical notch coupled with a posterior apical lip. Always be certain to follow the surface contour of the prostate.] **6**. With the tip of an index finger placed opposite to the posterior prostatourethral junction on one side and the tip of the Adson inserted to the raphe level on the other, palpate and appreciate the thickness of the raphe. The raphe should be palpated as a relatively thin partition posterior to the urethra. Sometimes, it may be a bit thicker. **7**. With the tip of the Adson, puncture the posterior raphe while lifting the urethra and make the tip of the Adson find the previously defined tract between the fascia and NVB on the opposite side. The NVB must not be caught between the index finger and the raphe, thereby damaging the NVB, which should be out of harm's way laterally. **8**. When the tip of the Adson is visible on the opposite side after the puncture through the raphe and it is clear that the tip of the Adson is above the NVB, bring the tip of a vessel loop, delivered by Mixter forceps from the first assistant, back through the posterior defect, thus isolating circumferentially the membranous urethra with its sphincter from the adjacent NVBs. (Tension on the vessel loop will define the posterior prostatourethral junction and allow traction of the junction upward and away from the rectum posteriorly. If the prostate is large, it may be necessary to replace the Adson with the tip of the larger Uppsala-Stille forceps [Stille] to grasp the vessel loop.) **9**. Have the first assistant use two Codman suction devices to keep the operative field dry, and have the second assistant press down in the midline with a sponge stick at the vesicoprostatic junction. In so doing, expose the anterior prostatourethral junction. **10**. Use the pointed Metz to cut transversely the striated urethral sphincter in its anterior half until the smooth muscle–elastic tissue wall of the membranous urethra is identified. The surface of this tissue appears somewhat corrugated with fibers running vertically. A skim of striated muscle is left on the prostate (just enough to prevent a positive margin). **11**. Use the long, blunt-tipped Metzenbaum scissors (blunt Metz) to rake back slightly the anterior prostate to further expose the urethral wall proximal to the transected anterior half of the striated sphincter. To expose still further the anterior urethral wall, insert a vein retractor to hold back the prostate gently and push the urethra posteriorly to loosen it slightly from the anterior prostate at the prostatourethral junction. **12**. Now make a transverse urethral wall cut 3 mm proximal to the proximal end of a well-visualized, striated urethral sphincter to expose the indwelling urethral catheter (Figure 8.3B). (The cut should be circumferential enough so that when the catheter is exposed, grasped, and pulled up out of the defect, there will be no anterior tear of the urethral stump.) After the initial transverse cut is established, place the vein retractor directly into the urethral lumen and apply gentle cephalad retraction to view the urethral lumen. Use the pointed Metz to cut the urethral wall on each side to an intact posterior half circumference. **13**. Now grasp and pull up with the Jones forceps a full loop of catheter through the anterior urethral wall defect. **14**. Clamp the catheter with two Shallcrosses side-by-side close to the prostate apex and transect the catheter between the forceps. The idea is to leave a short catheter end to be retracted into the bladder and a longer end to be exteriorized from the distal end of the incision. Tie each cut end of the catheter with No. 2 silk. First tie the distal longer end and then the shorter end. (The surgeon's knot tie on the proximal shorter end must be tight enough to keep the Foley balloon inflated.) **15**. Have the second assistant gently and distally retract the longer end of the catheter with its traction suture to further expose the posterior half of the urethra. (The retraction should not tear the anterior urethral stump. The distal traction suture is secured to the drapes with an Ochsner-Dixon forceps.)

POSTERIOR URETHRAL TRANSECTION

The aim in completing urethral transection at the apex of the prostate is to achieve a fully functional coapting residual urethral stump; i.e. to preserve urinary continence. This portion of the operation involves the principle that the distal continence mechanism begins at the verumontanum (veru) and that any urethral transection distal to the veru or distal to the apex of the prostate may compromise urinary continence in a subset of patients with short membranous urethras or posterior lips (see below). Loss of urinary control is the most alarming complication for patients undergoing radical prostatectomy. When the operation is performed correctly, the final urethral stump should protrude as a cylinder of tissue medial to the NVBs (Figure 8.4). The intact striated urethral sphincter fibers must remain inserted into the posterior raphe and not flail from detachment. Importantly, the proximal portion of the urethral stump may lie on a posterior lip of prostate that must not be incised or violated if the prostate is to be removed intact. The presence of a posterior lip should be suspected if an anterior apical notch is apparent during the anterior urethral transection.[11] If the dissection is not performed properly, the risk for a positive surgical margin at the transected posterior lip is immediately introduced. Remember that *there is always peril*

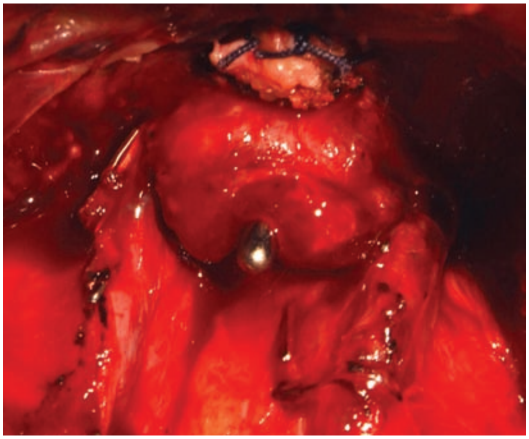

Figure 8.4 Urethral stump protrudes between neurovascular bundles.

at the apex because prostate cancer is frequently an apical disease. Fortunately, direct urethral invasion by cancer is uncommon.

Steps: 1. Now place the Stille posterior to the prostatourethral junction by following the course of the previously placed vascular tape (Figure 8.5A). (This step allows the NVBs to be out of harm's way and adds further support and elevation of the posterior prostatourethral junction above the underlying rectum.) **2**. Have the second assistant retract with a sponge stick in the midline at the vesicoprostatic junction as before. (The second assistant faces the head of the table, supporting the Stille with one hand and the sponge stick with the other. The first assistant uses two Codman suction devices to keep the field for the posterior urethral transection as dry as possible. The scrub nurse supports the vascular tape, which should be proximal to the posteriorly placed Stille.) **3**. With the team ready, place a No. 9 (sometimes No. 11 for larger prostates) Gil-Vernet retractor (Gil-Vernet) into the apical urethral opening to fully expose both the posterior half of the urethra to be transected and the seminal colliculus or veru. (The shorter-end catheter remnant should be retracted into the bladder lumen and not interfere with the Gil-Vernet during the posterior urethral transection). **4**. With the three assistants at their posts as described in Step 2, use the pointed Metz with curved tips down to release sharply the urethra laterally from the adjacent prostate at the 3 o'clock and 9 o'clock positions. Now transect the posterior urethral mucosa just distal to the veru and then the urethral wall to the prostate surface without cutting into the prostate (Figure 8.5B). Then by turning the curved tips upward, use the scissors to release the urethral wall in the midline and then finally at the junction of prostate and posterior raphe. (Variable quantities of striated urethral sphincter fibers will be visible lateral to the urethral wall as the raphe is approached. In the final release of fibromuscular fibers at the prostatourethral junction with curved tips of the scissors downward, the tape will become visible through the translucent veil of tissue to be finally transected just beyond the posterior midline prostate [Figure 8.5C]. During posterior urethral transection, prostate tissue is prominently soft and colored pale greenish white, whereas the urethra is firm and a pale yellowish white.) [**Note**: There is a pervasive misunderstanding that the final posterior urethral transection in radical retropubic prostatectomy includes the rectourethralis. *The rectourethralis is not part of radical retropubic prostatectomy*. However, it is very much a part of radical perineal prostatectomy. The rectourethralis is a fibromuscular complex situated distal to the apex of the prostate with midline attachment to the perineal body and centered on tissue between the bulbourethral (Cowper) glands, which are at the junction of the distal end of the membranous urethra and penile bulb. Both magnetic resonance imaging and midline sagittal histological findings confirm this.[10,12] If the rectourethralis complex is ever encountered in radical retropubic prostatectomy, the dissection has progressed too far posteriorly.]

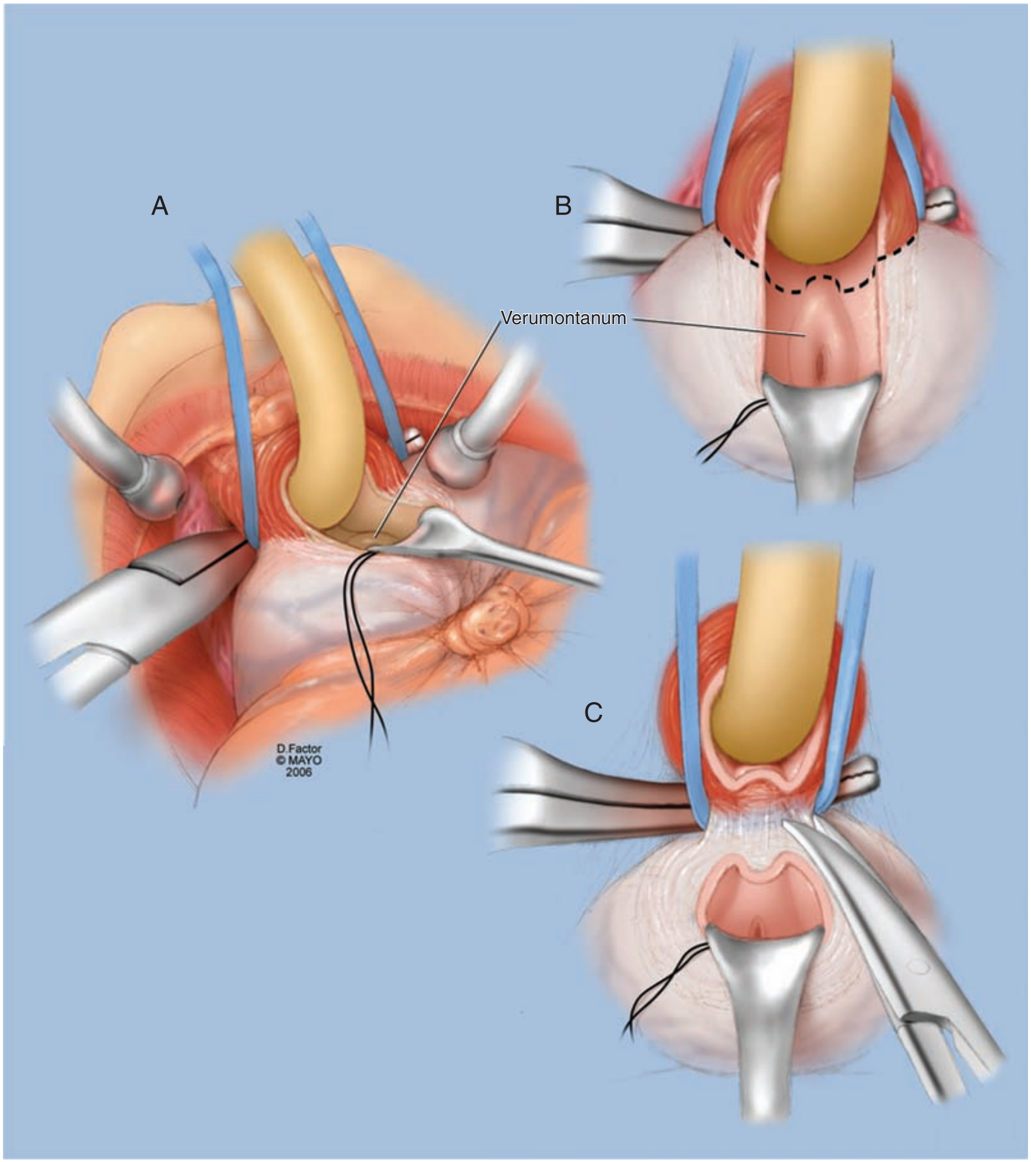

Figure 8.5 Posterior urethral transection. (A) Initial setup with vascular tape and Uppsala-Stille forceps supporting urethra and Gil-Vernet retractor used to expose veru. (B) Dashed line to begin transection of urethra without cutting prostate. (C) Final release of urethra at posterior apex using vascular tape as guide. (Used with permission of Mayo Foundation for Medical Education and Research.)

EXPOSURE OF THE PROSTATO-SEMINAL-VESICULAR FASCIA (DENONVILLIERS' FASCIA) AND NVBS DISTAL TO THE PROSTATE

Once the urethra has been transected, the prostate apex should be covered by fascia. Prostate tissue thickness at the apex in the posterior midline varies. If the apex is toroidal, there will be considerable posterior tissue. In other cases, the posterior prostate may taper to a thin rim. Great care is therefore always necessary in approaching the rectal surface after urethral transection. After urethral transection, shiny layers of Denonvilliers' fascia (DF) distal to the prostate in the midline should be obvious with extension of DF laterally as a continuous sheath to cover the anteromedial surfaces of the NVBs. [**Note**: For exposure of tissue beyond the posterior apex including the NVBs, have the second assistant retract with a sponge stick at the vesicoprostatic junction as before. The force applied to the sponge stick should be sufficient for viewing but not so strenuous that the NVBs are stretched or friable veins beneath the sponge stick on the anterior surface of the bladder are unnecessarily ruptured. If they bleed, use figure-of-eight 3-0 polyglactin on an SH taper needle or 5-0 poliglecaprone on the RB-1 taper needle for hemostasis.]

Steps: 1. Using the long, modified Jarit forceps (Jarit), break the sheath of DF into multiple bands. Working first in the midline, develop, cross-clip with 3-mm clips, and divide each fascial band. Clips are useful because they occlude associated tiny posterior veins, and the clipping serves primarily for hemostasis. Because there is usually more than one layer of DF distal to the apex, work layer by layer until the soft, yellow anterior surface of the rectum is apparent and there are no more layers of DF anterior to the rectal serosa in the midline. [**Note**: Now is the time to make a decision on the wisdom of intrafascial vs interfascial dissection as a component of NVB preservation (Figure 8.6).[10] If the dissection is to be electively intrafascial for greater NVB protection but less oncological safety, leave a layer of DF attached to the medial surface of the NVB. If dissection is to be interfascial for greater oncological safety but potentially less NVB protection – for example, to avoid a posterolateral cancer or clinical T2a nodule – carefully dissect DF off the medial surface of the NVB with the Jarit so that a layer of DF will cover the cancer. If the dissection is to be wide and unilaterally extrafascial to include the NVB with the prostate, the extrafascial plane is developed on one side before apical dissection.[8] In this case, cross-clip the NVB with 8-mm clips and divide the NVB distal to the apex of the prostate. If the dissection is to be wide and extrafascial bilaterally, the prostate is freed completely from the rectum before the apical dissection if it will free easily and is not stuck to the rectum.[8] [**Note**: Extrafascial dissections should be viewed as providing the greatest oncological safety but with the potential for the

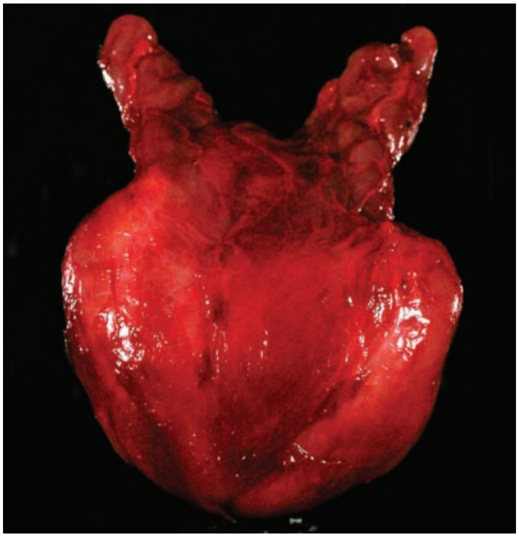

Figure 8.6 Radical retropubic prostatectomy specimen (posterior view), showing result of posterolateral interfascial dissection on left and intrafascial dissection on right.

least satisfactory functional outcome.] **2**. When the rectal surface is clearly exposed and identifiable by its yellow color due to associated adipose tissue, develop an area of rectal surface large enough to admit the tip of a sharply angled index finger to find the plane between the rectal serosa posteriorly and DF anteriorly. Make sure the tip of the index finger achieves a plane strictly parallel to the rectal surface. (The soft covering of DF on the posterior surface of the prostate should be appreciated with the index finger. If the correct plane of dissection is to be achieved, the gloved tip of the index finger must always be angled sharply cephalad. The nail of the index finger, allowed to grow to 2 mm in length, leads the dissection. Thus, the tip of the index finger provides acute tactile discrimination to know that the fingertip is adjacent to palpable DF anteriorly and not capsule, which has rough texture, denoting a mistake.) [**Warning**: This finger entry may be complicated by apical fibrosis or periprostatic inflammation from biopsy or antecedent transurethral resection of the prostate. During index finger mobilization, the anterior surface of the rectum should be visualized periodically. Make certain that the serosa of the rectum has not been violated with exposure of longitudinal smooth muscle of the rectal wall. If this happens, stop the finger dissection. Change the focus of dissection to lateral mobilization of NVB off one or both sides of the prostate adjacent and cephalad to the adherent apex. Once the correct plane between NVB and rectal surface is established laterally, this plane can be carried distally to the point where the smooth muscle fibers of the rectum have been previously exposed. This altered dissection technique will help to avoid entry into the rectal lumen with the tip of the index finger.]

NVB PRESERVATION

Release of the NVB should not begin without an understanding of the anatomy of the NVBs and how to recognize them. Each NVB contains many autonomic nerve fibers, some major (large caliber), some minor (small caliber), destined for the cavernous bodies. Because the NVBs are distributed around the curved posterolateral surface of the prostate, their distribution, in the axial plane, is crescentic with respect to the adjacent prostate. The bulk of the nerves, the larger ones, are usually centrally located within the NVB, but on occasion some may be positioned immediately adjacent to the crescentic surface and therefore subject to injury from hemostasis.[13] Smaller fibers generally are found along the tips of the crescent, one crescentic tip reaching up the lateral surface of the prostate, and the other tip extending toward the posterior prostate midline in association with DF. Nerves at the tips of the crescent are particularly subject to injury. Proximally, the NVB runs along the lateral surface of the seminal vesicle. The NVB is notably broad and thick in the region of the main vascular pedicle to the prostate at the vesicoprostatic junction, where many ganglionic connections of autonomic fibers to the bladder, seminal vesicles, and vasa deferentia are located. Distally, the NVB is primarily posterolateral with respect to the prostate. At the apex of the prostate, the NVBs may splay more anterolaterally and posterolaterally in juxtaposition to the adjacent urethral stump. In the presence of BPH the NVBs will be more posterior than lateral, and with small prostates with no BPH the NVBs will be more lateral than posterior. The aim is to save as many nerve fibers as possible and to avoid iatrogenic attrition by whatever cause.

How does one identify the NVB? Many NVBs have veins running parallel along their anterior surfaces, and by releasing the fascia that tethers the vein, the anterior edge of the NVB will fall laterally. Sometimes a small artery running parallel along the anterior NVB is a hallmark. If there is no telltale vein or artery, look for a soft tissue bulge on the lateral or posterolateral surface of the prostate arching convexly away from the lateral contour of the relatively firm prostate.

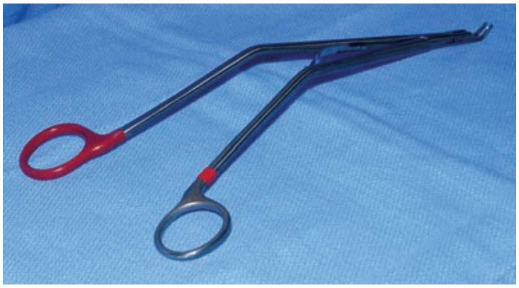

Figure 8.7 A 3-mm clip applier with 3-mm clip.

Steps: 1. Once the plane between DF at the prostate apex and the rectum has been entered, advance the tip of the index finger in the midline all the way to the point where the rectovesical pouch (cul-de-sac of peritoneum) begins or, in some cases, when fortunate, all the way to the junction of the prostate and seminal vesicles posteriorly, or even onto the posterior surface of the seminal vesicles. With the index finger, sweep bluntly and laterally to the palpable medial edge of each NVB at the lateral edge of DF. For efficiency and equal-force application posteriorly and laterally, *dissect ambidextrously*; that is, use the right index finger to sweep between DF and the rectal serosal surface toward the left NVB and the left index finger to sweep toward the right NVB. **2**. With an index finger inserted into the space between prostate and rectum to guide the dissection, free the NVB first distally opposite and lateral to the apex of the prostate unless there is so much adhesion, as noted above, that one is better off starting just distal to the main prostate vascular pedicle at the vesicoprostatic junction and working distally or finding a plane between the NVB and prostate laterally to reach the rectal surface. Start release of the NVB adjacent to the apex by transecting the levator fascia (lateral pelvic fascia) on the sides of the prostate with fine forceps or curved scissors passed retrograde or antegrade in a line anterior and parallel to the NVB. If there is any apparent fascial vascularity, use 3-mm clips. To some degree, levator fascia that remains on the lateral surface of the NVBs protects the freed portion of NVBs from tension injury. Great care must always be exercised not to stretch the NVBs. **3**. Use 3-mm clips and clip applier (Figure 8.7) to secure the tiny micropedicles (arteries, veins, and nerve branches) sporadically emanating along the anterior NVB edge which tether the NVB to prostate fascia and capsule. **4**. For the recommended mirror-image ambidextrous technique described herein (Figure 8.8), use an instrument (Jarit or the modified curved scissors with sharp tip on blunt tip) in the right hand to dissect, working in retrograde fashion, the right NVB while the left index finger and thumb palpate the right posterolateral prostate. This step provides continuous, critical sensory (haptic) feedback for the presence of cancer and the ability to keep cancer nodules away from the NVB. On the left side of the prostate, do the opposite; that is, dissect the left NVB off with an instrument in the left hand and use a posteriorly placed right index finger between rectum and prostate and the right thumb on the left lateral surface of the prostate so that palpation is possible along the left posterolateral prostate as the NVB is rendered free after securing each micropedicle. The NVBs should progressively drop away as the dissection proceeds proximally. **5**. Work methodically from side to side to free the NVBs. In so doing, one avoids damage from tension to the contralateral NVB as dissection is proceeding on the ipsilateral side. Tension may even fracture the contralateral NVB. *Remember that the NVBs are delicate and will tolerate neither stretch nor shear*. **6**. To minimize encroachment of the fine nerves running along the surface of the NVB, use 3-mm clips and 3-mm clip applier whenever possible and the larger 6-mm clips when necessary to secure each micropedicle. Carry the NVB mobilization on each side cephalad to the main prostate pedicle and then stop. [**Note**: There is no need to use electrocautery near the NVB during NVB preservation.[14] However, if the anterior edge of the NVB is defined by a prominent vein tethered to the visceral prostatic fascia, the fascia must be disrupted

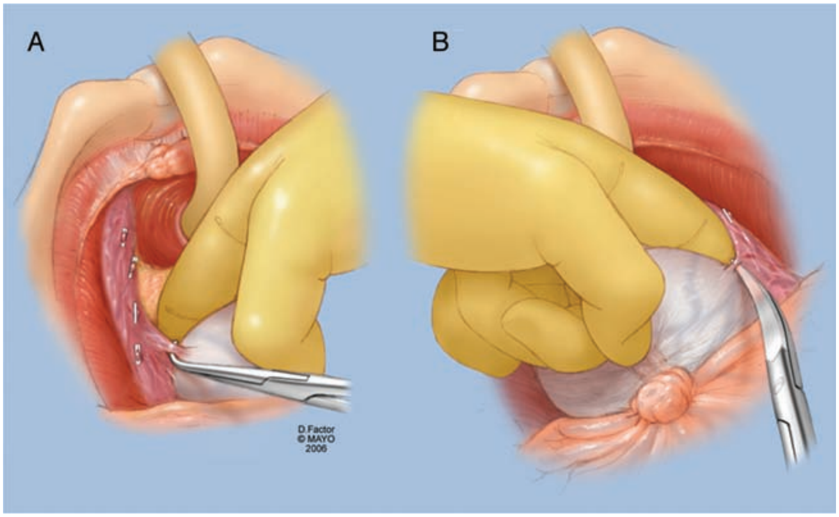

Figure 8.8 Neurovascular bundle preservation. (A) Left side of prostate. Use of modified Mixter petit-point forceps to isolate micropedicle for 3-mm clip application. (B) Right side of prostate. Use of curved scissors for similar isolation. (Used with permission of Mayo Foundation for Medical Education and Research.)

in some fashion so that the NVB will fall away laterally without rupturing the vein. If the vein cannot be dislodged with fine forceps used bluntly, try greatly reduced electrocautery energy level at a setting of '10' (when '40' is generally used for routine hemostasis) and lightly tap the prostatic fascia in a line 2–3 mm anterior to the vein and removed from the course of the NVB. Then use a Kittner dissector gently on the surface of the relatively soft NVB to roll the vein and NVB away. This technique is often successful when neither forceps nor curved scissors suffice to move the NVB without inadvertent capsulotomy.]

PERITONEAL CUL-DE-SAC DETACHMENT AND INTERVAL HEMOSTASIS

Steps: **1**. Before proceeding further with ligation of the prostate vascular pedicle, pause to retract with an index finger the apical prostate cephalad just enough and without tension on the NVBs so that the point of posterior attachment of the peritoneal cul-de-sac is visible. **2**. Ask the first assistant to grasp the midline rectal serosa with Selman forceps and retract distally. **3**. Use the blunt Metz to open transversely the attachment to create a space posterior to DF covering the seminal vesicles. Once this space has been created, the space is widened by spreading laterally with an index and a middle finger so that the index finger can then guide very precisely the transection of the vascular pedicle anterior to the NVB. **4**. For added distal periurethral stump hemostasis, remove the distal Foley catheter remnant that had been placed on mild tension. Place a new lubricated catheter into the urethra and, once in the retropubic space, thread its tip through a hole in the middle of two dry absorbable gelatin sponge, USP, pledgets (4 × 5 cm). After inflating the balloon to 8 ml and cutting off the tip of the Foley catheter just short of the balloon, apply traction on the catheter for the purpose of temporary, distal absorbable gelatin sponge, USP, tamponade to stop venous ooze from the pelvic floor. **5**. Finally, inspect the surface of the prostate and use the DeBakey-Dietrich forceps and 6-mm clips or 5-0 poliglecaprone suture to stop active bleeding.

ISOLATION AND TRANSECTION OF THE PROXIMAL RUNOFF OF THE DVC

From the proximal bunching suture still in place at the bladder neck, identify the swath of veins that is the proximal runoff of the DVC passing laterally and posteriorly toward the internal iliac veins. These veins are primarily pudendal and partially obscure the underlying vascular pedicle to the prostate. They are the proximal end of the hyperbola of pudendal veins (mentioned above) or Santorini plexus draped over the prostate lateral to and beneath the detrusor apron or simply the vesicopudendal plexus of the *Jena Nomina Anatomica*.[15]

Steps: 1. Probing with the Jarit from above and passing it toward and anterior to the prostate vascular pedicle, lift and isolate the bundle of veins on each side. There also may be some small associated arteries in the bundle. **2**. Doubly clamp the bundle with two Shallcrosses (Figure 8.9A), then transect and ligate with 2-0 polyglactin. If the vascular bundles are relatively large, use a suture ligature of 3-0

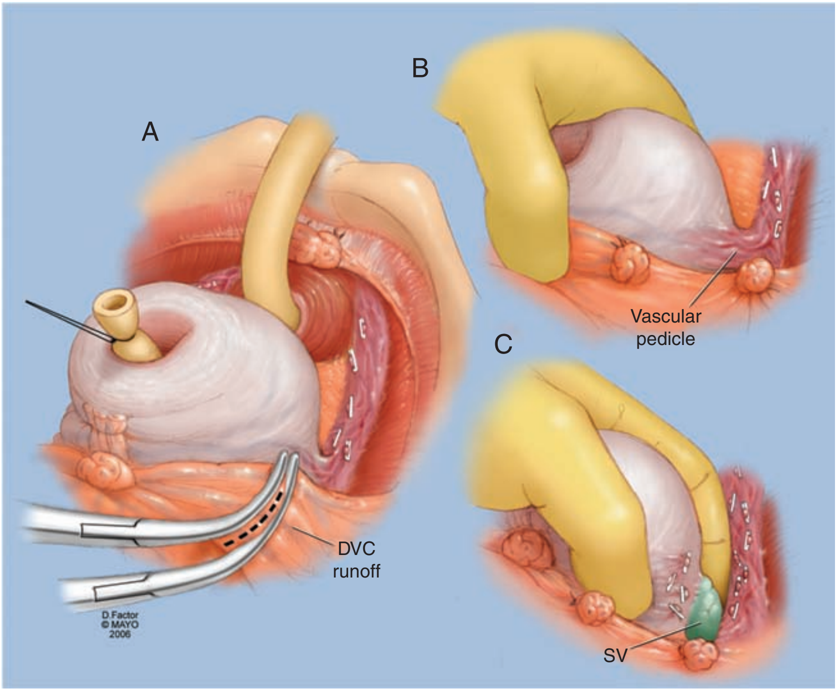

Figure 8.9 Cross-clamping of proximal dorsal vein complex (DVC). (A) Shallcross forceps in place with dashed line of division to fully expose main vascular pedicle to prostate. (B) Pedicle exposed after Shallcross clamping, tying, and transection of proximal DVC. (C) Exposure of lateral seminal vesicle (SV) after vascular pedicle transection. (Used with permission of Mayo Foundation for Medical Education and Research.)

polyglactin on the proximal tissue. If the vascular bundles are relatively small, 10-mm clips pressed firmly may suffice without the need for ligation. (Double clipping proximally is advisable with single clipping distally to prevent back bleeding. Remember not to cut too close to the clip because clips tend to come off easily if they do not contain sufficient tissue. This maneuver exposes the vascular pedicle to the prostate [Figure 8.9B] and makes it much easier to isolate and divide the pedicles anterior to the NVB. Furthermore, the seminal vesicles are much more easily freed from the contiguous NVBs and pelvic plexus on each side.)

VASCULAR PEDICLE LIGATION AND DIVISION

Steps: **1**. With an index finger supporting the pedicle and the thumb rotating the prostate slightly in the axial plane, use a Jarit or Adson to separate the pedicle tissue into small bundles. **2**. Clip the bundles with 3-, 6-, or 8-mm clips, and transect each bundle using curved scissors. (It should be perfectly obvious where the NVB is located so that pedicle ligation and division is visibly anterior to the course of the NVB.) Carefully continue the process of bundle isolation and transection until the lateral surface of each seminal vesicle is exposed (Figure 8.9C).

DISSECTION AND FREEING OF THE SEMINAL VESICLES

At this point the posterior surfaces of the seminal vesicles should be covered by DF. Place the patient in the Trendelenburg position for this part of the procedure.

Steps: **1**. Without puncturing the seminal vesicles, use the Jarit or Adson to raise DF off the posterior surface of the seminal vesicles at least midway toward their tips. **2**. Proceeding all the way from one side to the other until the tips of the seminal vesicles are fully visible, apply clips, 3 mm or 6 mm, to DF and small vessels. **3**. Open fascia in the midline between the vasa deferentia and, sweeping with tip of Adson or Shallcross behind each seminal vesicle, create a plane that will admit the tip of an index finger. **4**. Grasp the seminal vesicle and ampulla of vas deferens (vas) together with thumb and forefinger to provide mild traction. **5**. Use the Jarit or Adson to isolate, clip with 3-mm clips, and transect the numerous seminal vesicle arteries that enter laterally and at the tip of the seminal vesicle. **6**. Use the Adson for larger vascular bundles, in particular the constant vascular pedicle between the seminal vesicle and ampulla of the vas. Use 3-, 6-, and 8-mm clips accordingly. **7**. Tease with the tip of the Adson the tip of the seminal vesicle out of the depths after most of the seminal vesicle vessels have been isolated and transected. **8**. Once the tip of the seminal vesicle is sufficiently mobilized with the Adson, use an index fingertip to continue the process. As additional pedicle tissue posterior and lateral to the seminal vesicle is appreciated, cross-clip and divide it with 3-, 6-, or 8-mm clips. **9**. When all of the vessels have been secured and the seminal vesicle is free, free the vas and cross-clip it with a 10-mm clip with just enough pressure to occlude but not incise the vas. Transect the vas as close to the tip of the seminal vesicle as possible. (Sometimes, it is useful to secure the vas and transect it before seminal vesicle mobilization, depending on what side one is working on.) [**Note**: If the seminal vesicles are stuck from inflammation or vertically disposed in a deep narrow pelvis, consider transecting the seminal vesicle at midpoint, taking out the remainder of the seminal vesicle later so as not to injure the adjacent NVBs. *For pelvic plexus and NVB protection, the seminal vesicle should always be dissected medially away from the NVB whether attached to or detached from the prostate at the time of mobilization*.]

REMOVAL OF PROSTATE FROM BLADDER NECK

Steps: 1. Face the foot of the table and retract the seminal vesicle tips together upward and proximally to expose the posterior junction of the seminal vesicles and bladder. **2**. Use sharp scissors or cautery to start posterior separation of the seminal vesicles from bladder distal to the trigone. (The posterior serosa of the bladder as it approaches the posterior vesicoprostatic junction has a parabolic shape with the tip of the parabola defining the most distal underlying trigone. If there is a median lobe of prostate, attempts to find the right plane will be difficult, and attention should be transferred immediately to finding the anterior vesicoprostatic junction.) **3**. Now face the head of the table and support the prostate with an index finger across the posterior vesicoprostatic junction. **4**. Cut and remove all proximal bunching sutures. Use the shorter blunt Metz (Pilling Weck) to begin to transect sharply the prostate from the bladder anteriorly (Figure 8.10A). Use the sharp edge of each blade of the scissors to sweep from right to left and vice versa to develop the plane between bladder and prostate. **5**. Use electrocautery for arterial bleeding. **6**. Develop the plane down to the vesical or prostatic urethral mucosa exiting from the bladder lumen. Make a transverse cut to expose the short end of the catheter, which is then retracted cephalad by the first assistant. **7**. Place the tip of an index finger into the bladder lumen to define the vesicoprostatic junction laterally and enlarge the bladder opening with electrocautery until the short end of the catheter with the inflated balloon can be removed. **8**. Grasp the opened bladder wall with two Adair forceps placed at 2 and 10 o'clock to examine the interior of the bladder. Look for bladder mucosal lesions if the patient has not undergone preliminary cystoscopy. Observe the trigone and the orifices, and make sure that spurts of urine emanate from each orifice. **9**. With the index finger of one hand supporting the posterior vesicoprostatic junction, transect the remaining posterior attachment of prostate to bladder by making the cut parallel to the bladder wall and distal to the ureteral orifices, which are always kept within view during the

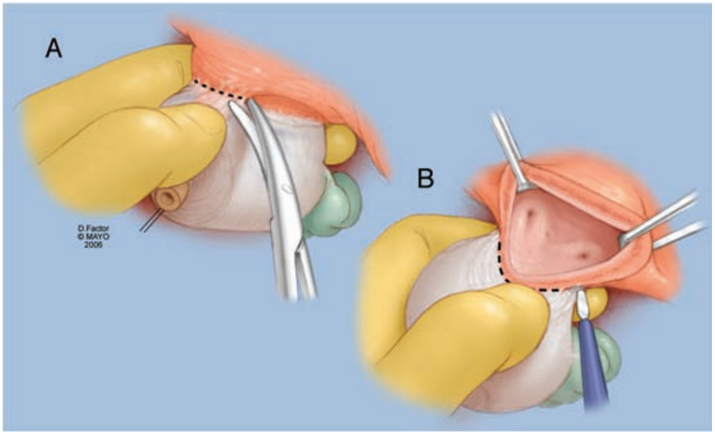

Figure 8.10 Prostate removal with posterior index finger support. (A) Scissor dissection while holding prostate and seminal vesicles. (B) View into bladder lumen with visualization of ureteral orifices before completing transection of bladder neck along dashed line with monopolar electrocautery. (Used with permission of Mayo Foundation for Medical Education and Research.)

transection (Figure 8.10B). (With interfascial dissection, the final prostate specimen can be suitably invested by fascia for oncological safety while NVBs and urethral stump for anastomosis are well preserved [Figure 8.11]). **10**. To aid mucosal eversion, place a 12-o'clock traction suture of 3-0 polyglactin into full-thickness bladder neck, including 1 cm of vesical mucosa. **11**. Remove the two Adair forceps. **12**. Grasp the ends of the traction suture with Ochsner-Dixon forceps, securing the traction suture to the proximal end of the central Balfour blade or wrapping it around the central wing nut to put the bladder opening on proximal tension for bladder neck reconstruction.

BLADDER NECK RECONSTRUCTION

The bladder neck as a sphincter becomes defunctionalized as a result of vascular pedicle ligation and prostate removal; it never resumes its normal smooth muscle sphincteric capacity once healing takes place. Eventually the new bladder neck will become a fixed opening that should not be rendered obstructive in the sense

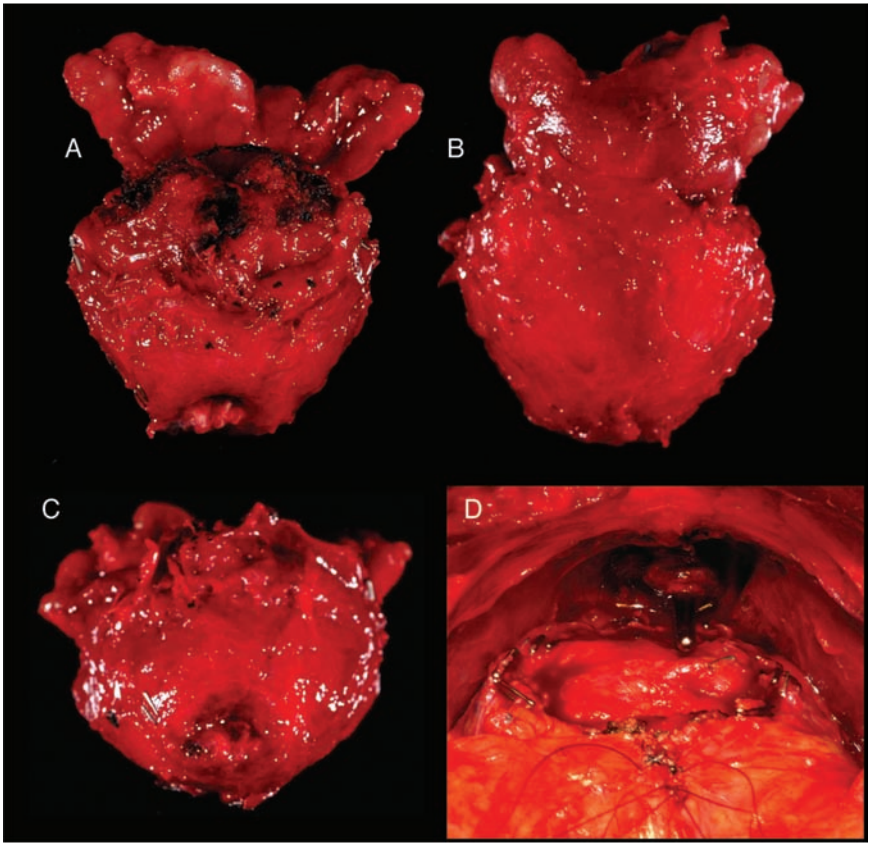

Figure 8.11 Final radical retropubic prostatectomy specimen (prostate and seminal vesicles). (A) Anterior. (B) Posterior. (C) Apex. (D) Bladder foreground, neurovascular bundles laterally, and urethral stump distally after removal of same specimen that is margin-negative and well invested by fascia after interfascial neurovascular bundle-preserving technique.

of unnecessary contracture. The goal then is to make the opening of appropriate caliber that will satisfactorily match the caliber of the urethral stump below. If the opening is too small, subsequent vesical neck contracture is invited. If the opening is too large, the urethral stump will be splayed open and the urethral stump consequently foreshortened because of reduced residual functional urethral length.

Steps: 1. Using continuous Lembert suture technique, evert the vesical mucosa of the anterior half of the bladder neck opening with running 3-0 poliglecaprone. **2**. Then use a single everting 2-0 polyglactin suture at 6 o'clock to the proposed new bladder neck to create anteriorly the proper new bladder neck caliber that will accommodate a 26-Ch Otis bulb or bougie-à-boule as tested by a pop-in, pop-out sensitivity. (If the anterior bladder wall is not too thin and there are residual anterior longitudinal detrusor fibers sweeping anteriorly around the bladder neck [bundle of Heiss[16]], a new bladder neck can be constructed with everted mucosa that incorporates these fibers, thereby achieving a measure of temporary passive urinary continence during the early healing period.) **3**. For a large bladder neck opening, close the posterior bladder neck defect in a Y-plasty using multiple interrupted, figure-of-eight 3-0 polyglactin sutures on the RB-1 taper needle (Figure 8.12A). The Y-plasty will recreate a trigone. If the posterior transection of prostate from bladder comes close to the ureteral orifices, cannulate each orifice with a No. 5 feeding tube. Start the Y-plasty with two or three interrupted sutures on each side to recess the orifices, then remove the feeding tubes, and proceed as above. (If the posterior defect is tiny, a simple racquet plication will suffice with running or interrupted 3-0 polyglactin.)

ANASTOMOSIS

Urine leak is avoided by proper suture placement and contracture minimized by not using too many sutures, which may produce ischemia and a ring of fibrosis. Sutures should not be placed so that adjacent levator ani muscle of the pelvic floor is incorporated into the anastomosis. Such a maneuver will simply defunctionalize muscle that may be important in Kegel exercise and support of the new vesicourethral anastomosis. The second assistant applies perineal pressure with a sponge stick between the pubic arch to make the urethral stump more visible and accessible for the anastomosis (see Figure 8.12).

Steps: 1. Place four 2-0 poliglecaprone sutures on CT-2 taper needles into the bladder neck at 2 and 10 o'clock anteriorly and at 5:30 and 6:30 posteriorly. (Subsequent urine leaks are most typically at 6 o'clock, so the 5:30 and 6:30 sutures are most important in closing any potential space in the anastomosis posteriorly.) **2**. Make certain that hemostasis is satisfactory along each nerve bundle, the bladder neck, the pelvic side walls, and obturator spaces. (Along the NVB it may be necessary to use 5-0 poliglecaprone and 3-mm and 6-mm titanium clips placed after grasping the bleeding point with the tip of the DeBakey-Dietrich forceps. For the 6-mm clip, a true right-angle clip applier is used. If there is bleeding between clips, use 5-0 poliglecaprone to make a 'clip sandwich' that will compress and stop the offending bleeder between the clips. The suture should be passed very close to the underside of the clips so that the needle does not enter the NVB more than necessary.) **3**. Without tension on the adjacent NVBs, have the first assistant use a sponge stick to depress the rectum between the NVBs close to the bladder. **4**. Adjust the patient into reverse Trendelenburg position with a slight tilt toward the surgeon, and lower the table. **5**. With fine-caliber CT-2 taper needles bent slightly against the thumb tip into a 5/8-circle configuration before passing through stump tissue, place the posterior distal sutures at 5 and 7 o'clock. Aided by perineal pressure, the stump should protrude as a cylinder so that

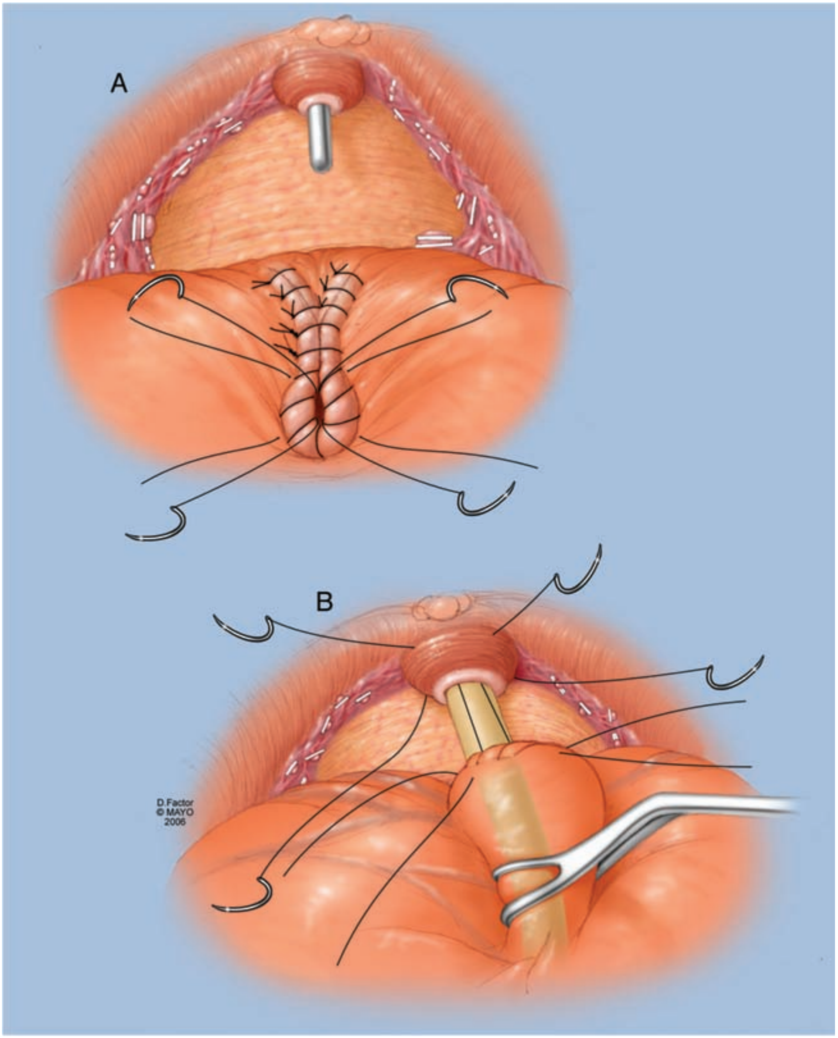

Figure 8.12 (A) Bladder neck reconstruction and placement of sutures for anastomosis. (B) Grasp Foley catheter with modified Babcock forceps through anterior bladder wall as an aid to approximating new bladder neck to urethral stump. (Used with permission of Mayo Foundation for Medical Education and Research.)

the sutures at the 5 and 7 o'clock positions pass medial to the adjacent NVBs. This step is aided by the first assistant's skillful lateral retraction of the NVBs with the plastic suction tip. Both anteriorly and posteriorly, use forehand for the 'far' sutures and backhand for the 'near' sutures. Face the head of the table to place the two posterior sutures, and face the foot of the table to place the two anterior sutures. (The needle is turned approximately 135° to the direction of the needle driver for all four sutures whether forehanded [near sutures] or backhanded [far sutures]. When properly placed, the sutures distally include full-thickness urethral wall and a few millimeters of striated sphincter with sufficiently strong bites so that subsequent bladder spasm will not disrupt the anastomosis.) **6**. Once the posterior sutures have been placed, introduce a 20-Ch all-silicone catheter retrograde through the urethra and reconstructed bladder neck. Inflate the balloon to 11 ml to guarantee 10 ml in the balloon. If there is any resistance noted in the navicular portion of the urethra reflecting limited urethral caliber, use the Otis urethrotome to enlarge the urethral lumen at 12 o'clock to 24 Ch. **7**. Relax the Balfour blades so that the bladder neck can be apposed to the urethral stump without tension. Approximately 4–5 cm proximal to the reconstructed bladder neck, use the bent Babcock forceps to grasp the Foley catheter through the wall of the bladder and distal to the balloon (Figure 8.12B). This avoids the encumbrance of having to tie over a balloon, resulting in a possibly less secure, less watertight anastomosis. During the tie-down, have the first assistant hold the bent Babcock to push the new bladder neck against the urethral stump while the second assistant applies perineal pressure to bring the stump into better view to facilitate approximation of bladder neck and urethral stump. **8**. Because the anterior sutures are the strongest in terms of tissue holding them, tie them first. Then tie the more tenuous posterior sutures. During the tie-down of each knot, set the down-hand into-the-wound index finger approximately 1 cm distal to the intended knot and cinch or tighten each throw with the up-hand out-of-the-wound index finger. (Because a force vector will be applied toward, not away from, the urethral lumen, the fingernail of the down-hand index finger should face the knot or the urethral lumen for the most secure knot possible.) [**Note**: If for some reason the bladder cannot be approximated without tension against the urethral stump, the bladder can be lengthened anteriorly to gain the necessary length by closing vertically a transverse bladder wall incision 5 cm long and made 5 cm proximal to the bladder neck.]

Final steps: 1. Irrigate the wound with triple antibiotic solution. **2**. Place closed suction 1/4-in.-diameter plastic drains into each obturator space with the drain ends curled cephalad and upward and not allowed to rest in proximity to the anastomosis. **3**. Secure each drain with suture to the skin on either side of the wound. **4**. Close the fascia with running doubled 0 polydioxanone in two lengths, the first suture from the distal end of the incision to half to two-thirds of the way proximally, and the second from the proximal end of the incision to meet the first suture. Just before tying, split the doubled suture into two strands, passing one strand through the preceding loop, which is then lowered on tension with the curved or angled tip of a pair of suture scissors. Then make the usual tie-down with the two separated strands and 6–8 throws squared. **5**. Close subcutaneous tissue with running 2-0 polyglactin on a CT-1 taper needle and the skin with running subcuticular 3-0 poliglecaprone on a PS-1 reverse cutting needle. [**Note**: Drains with closed-system receptacles are left in until there is less than 20 ml of output over 48 hours. If the drains do not meet this test on suction for 21 days, the suction receptacles are removed. The skin sutures are removed. The drain tubes are cut to appropriate length and placed in pediatric-size plastic drainage bags that stick to the skin. This new system is used until the above criteria are met. If there is suspicion of urine leak, a drainage fluid creatinine test is ordered. If the drainage is not copious, the drains can be advanced 5 cm to encourage diminution in output. Patients take an oral fluoroquinolone (if they are not allergic) during the time of indwelling catheterization and drain placement and for 3 days beyond removal of the catheter. The catheter is left indwelling for 18–21 days, based on the wound-healing principle of allowing full collagenization and some collagen remodeling and strengthening at the anastomosis. This program usually obviates any need and bother for catheter reinsertion and cystography. The catheter is made more comfortable by liberal application of triple antibiotic ointment and 1% hydrocortisone cream at the external urethral meatus and of lubricating jelly applied regularly along the catheter proximal to the meatus to reduce discomfort while walking.]

ACKNOWLEDGMENTS

Special people have sparked my interest and background for this chapter during my professional life and I thank them all. In particular, I include David C Utz, for stimulating my original interest in prostate cancer and the concept of continuous technical improvement in the various aspects of radical prostatectomy; Donald R Cahill, Professor of Anatomy, for teaching me the complexity of pelvic floor anatomy; Patrick C Walsh, for surgical concepts of DVC control, NVB preservation, bladder mucosal eversion, 'pillar' tissue, and the switch from 2.5- to 4.3-power loupes to bring visual capability into the realm of laparoscopy; Peter T Scardino, for vertical continuous suture technique for emergency DVC control; Kenichi Tobisu, for use of an instrument (bent Allis forceps) rather than fingers for the 'bunching' technique; Eduardo Kleer, as Urology Resident, for convincing me that only four interrupted sutures are necessary for a consistently watertight mucosa-to-mucosa vesicourethral anastomosis; Hartwig Huland, for demonstrating 5-0 suture for NVB hemostasis, when necessary, in addition to titanium clips; and Christian Barré, for promoting use of 3-mm clips instead of 6-mm clips along the NVB. Finally, I express profound gratitude to my colleagues in the Department of Urology at Mayo Clinic, including staff physicians, residents-in-training, and postgraduate uro-oncology fellows, who have added to my insight about radical prostatectomy since July 1968, when I began my own residency training program in urology under Ormond S Culp, then chair of the department. Medical illustrations were created by David A Factor MS. Steven R Rettke, staff anesthiologist, reviewed the subsection 'Anesthesia, Analgesia, and Medications.'

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Appendix A Operating room: team and conditions

Operating room team

1. Surgeon (urologist)
2. First assistant (urology resident)
3. Second assistant (certified surgical assistant)
4. Certified surgical technologist as scrub nurse to hand instruments as requested
5. Registered nurse as 'circulator'
6. Certified registered nurse anesthetist
7. Anesthesiologist

Operating room conditions

1. Room of suitable size is well lighted, kept relatively quiet to minimize surgeon fatigue, and warm enough to prevent patient hypothermia
2. Communication is courteous at all times between all team members
3. Titanium clips are requested by package color for the size needed. For example, a request of 'green angled' means 8-mm clip on an angled applier (Appendix B)
4. The operation proceeds smoothly when the scrub nurse is flawless in instrument-table organization, knows every step of the procedure and what to expect, and makes no mistakes in instrument delivery

Appendix B Instruments and other supplies[a]

Instrument	*Purpose*	*Catalog number*[b]
Forceps		
Adair 9 in.	Grasp bladder neck	CH1565
Adson 8½ in.	Dissection	NL3510
Allis 10 in.	Grasp bladder neck	CH1560
Babcock 8 in.	Grasp seminal vesicle tip	SU5001
Carmalt 8 in.	Grasp Kittner	SU2777
DeBakey 9 in., 2-mm tip	Grasp bladder mucosa	CH5904
DeBakey-Dietrich, 1-mm tip	Hemostasis	30-8133 (Codman, Raynham, Massachusetts)
Evans 9¾ in.	Grasp silk suture	SU2465
Ferris Smith 6¾ in.	Grasp fascia	SU2511
Gemini 11⅛ in.	Cut down on dorsal vein complex	19-5583 (Codman)
Halsted Mosquito, 5 in.	Tag anterior anastomotic suture	

Appendix B Instruments and other supplies[a]—cont'd

Instrument	*Purpose*	*Catalog number*[b]
Curved		SU2702
Straight		SU2700
Jones 11½ in.	Grasp catheter from urethra	19-8152 (Codman)
Mixter 10½ in.	Grasp vascular tape and suture	CH1726
Mixter petit-point (modified) 10¾ in.	Dissection	140-223 (Jarit, Hawthorne, New York)
Myers-Babcock 9½ in.[c]	Bunching, hold catheter	GU8600
Ochsner-Dixon 6¼ in.	Grasp fascia	SU2820
Rochester-Carmalt 12¼ in.	Sponge stick	30-8092 (Codman)
Rochester-Rankin 6¼ in.	Grasp peritoneum, bleeders	SU2740
Selman 10 in.	Grasp bladder mucosa	351842 (Pilling Weck, Fort Washington, Pennsylvania)
Shallcross 8 in.		SU10510
Singley 9¾ in.	Remove adipose tissue	SU5075
Uppsala-Stille 9¾ in.	Support urethra	107-1058-241 (Stille, Solna, Sweden)
Needle drivers		
DeBakey cardiovascular 10⅜ in.		CH2483
Masson 10½ in.		CH2440
Scissors		
Metzenbaum	Dissect prostate from bladder	
9¼ in.		141469 (Pilling Weck)
11 in.		
Blunt-tipped		CH2020-001
Sharp/sharp-tipped		CH2020-001-modified
Satinsky 9¾ in. (modified sharp tip over blunt tip)	Cut tissue	CH5650
Vital Mayo 9 in.	Cut suture	CH2096
Retractors		
Balfour center bladder blade		SU3022
Balfour wide blade with 'wings'		(Not marketed)

Continued

Appendix B Instruments and other supplies[a]—cont'd

Instrument	*Purpose*	*Catalog number*[b]
Balfour with blades		SU3060
Dixon malleable center blade		SU3030
Gil-Vernet		
No. 9		GU8770
No. 11		GU8771
Vein retractor 9¼ in., 1 cm wide		(Maker unknown)

Titanium clips and appliers[d]

Clip size, mm	*Clip applier*	*Catalog number (container color)*
10 Large	Straight	437111 (orange)
	Angled	437115 (orange)
8 Large-medium	Straight	337411 (green)
	Angled	337115 (green)
6 Medium	Straight	237111 (blue)
	Angled	237115 (blue)
3 Small	Straight	137112 (red)
	Angled	137117 (red)

Suture[e]

Type	*Size*	*Catalog number*	*Needle*
Poliglecaprone (Monocryl)	2-0	y317	SH taper
	3-0	y316	SH taper
	3-0	y936	PS-1 reverse cutting
	5-0	y303	RB-1 taper
Polydioxanone (PDS)	0	z990	CTX taper
Silk	0	678	FSL reverse cutting
	2	sa8	None
	2-0	sa85	None
	3-0	sa74	None

Appendix B Instruments and other supplies[a]—cont'd

Type	*Size*	*Catalog number*	*Needle*
Polyglactin (Vicryl)	0	j270	CT-2 taper
	1	j335	CT-2 taper
	1	j359	CT
	2-0	j333	CT-2 taper
	2-0	j615	None
	2-0	j259	CT-1 taper
	3-0	j305	RB-1 taper
	3-0	j416	SH taper

Other supplies
Optical loupes: 4.3 power with maximal focal length (Surgical Acuity, Middleton, Wisconsin)
Headlight (CUDA Products Co., Jacksonville, Florida)
Headlight source (Xenon Series 9000, Model 9300 Luxtec Corp., Worcester, Massachusetts)
Operating room table (Skytron Elite 6500, Skytron, Grand Rapids, Michigan)
Four overhead operating room table lights: (ALM, Getinge USA, Inc., Rochester, New York)
Gelfoam No. 100 (Ferrosan Surgifoam, Johnson & Johnson, New Brunswick, New Jersey)
Otis bulb GU4005-026
Otis urethrotome GU4140
Van Buren sound GU4010-018
Stainless steel blade (Bard-Parker BD Medical, Franklin Lakes, New Jersey)
  No. 10
  No. 15
  No. 20
Catheter, silicone-coated latex 20-Ch 30-ml balloon Bard 'Foley catheter' (CR Bard, Inc., Murray Hill, New Jersey)
Catheter, silicone 20-Ch 10-ml balloon (Tyco Healthcare, Kendall Co., Mansfield, Massachusetts)
Drains, Jackson-Pratt round 5.0/15F (Cardinal Health, Inc., Dublin, Ohio)
Drain reservoir for closed system (Bard 'suction evacuator') (CR Bard, Inc., Murray Hill, New Jersey)
Dressing (Steri-Strips ¼ in., 3M Healthcare, St. Paul, Minnesota)
Gloves (Sensi-Touch, Ansell Healthcare, Inc., Dothan, Alabama)
Kittner sponge/blunt dissector 30-101 (DeRoyal, Powell, Tennessee)
Suction (single), Yankauer (26 cm – 10½ in.) with hole, plastic (Cardinal Health, Inc., Dublin, Ohio)
Suction (pair), Andrews-Pynchon suction tube 70-6560 (Codman, Raynham, Massachusetts)

Continued

Appendix B Instruments and other supplies[a]—cont'd

Vesseloop, white, 15 in. 8888-585232 (Sentinel Loops, Sherwood-Davis & Geck, Tyco Healthcare, Mansfield, Massachusetts)

Electrocautery unit (Pfizer Valleylab Force FX, Model No. E-8006 with 10-in. length monopolar wand, Tyco Healthcare, Valleylab, Boulder, Colorado)

Irrigation: 250 ml normal saline with neomycin 125 mg, polymyxin 25 mg, and gentamicin 20 mg

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[a] The purpose of this Appendix is to provide information only with respect to what equipment is used. The list should not be construed in any sense as product endorsement.

[b] Unless specified with names of companies in parentheses, catalog numbers are from V Mueller, Cardinal Health, Inc., Dublin, Ohio.

[c] Potential conflict of interest because author has royalty arrangement with Cardinal Health for this modified Babcock forceps through Mayo Medical Ventures, Rochester, Minnesota.

[d] Horizon surgical titanium clips, Weck Closure Systems, Research Triangle Park, North Carolina.

[e] Ethicon, Inc., Cornelia, Georgia; Somerville, New Jersey; San Angelo, Texas.

CHAPTER 9

Nerve-sparing radical prostatectomy

Paolo Gontero and Roger S Kirby

ANATOMICAL REMARKS

A precise knowledge of the neurovascular anatomy of the prostate is an essential prerequisite for a nerve-sparing (NS) approach to radical prostatectomy (RP). This has been excellently described by Walsh and co-workers[1,2] as reported in Chapter 2 of the present book. The caudal portion of the pelvic plexus, located at the tip of the seminal vesicles, emanates autonomic fibers that form a dense network with the described vessels.[3,4] Some of them perforate the prostatic capsula to enter the substance of the prostatic gland. These branches are inevitably sacrificed during an NS approach, but it is believed that they do not contribute significantly to erectile function. The majority of nerve fibers, known as the cavernous branches, travel in a direct route from the pelvic plexus toward the posterolateral base of the prostate, gradually coalescing from a group of fibers approximately 12 mm wide to a more organized bundle approximately 6 mm wide at the level of the prostate. At this point, they lay just underneath the lateral pelvic fascia, between the levator fascia and the prostatic fascia (a fibrous layer in direct continuity with the true prostatic capsule). At the level of the membranous urethra they are located at the 3 o'clock and 9 o'clock position, just beneath the striated sphincter that at this point surrounds both the urethra and the prostatic apex.

By studying the development of cavernosal nerve fibers in fetuses of different gestational age, Lunacek et al[5] found that the neurovascular bundles (NVBs) run dorsolateral to the future prostate only in the early gestational phase (within the 10th week). Thereafter, as the prostate begins to develop, the nerve fibers are displaced more anteriorly, along the convex surface of the prostatic capsule, assuming the shape of a 'concave curtain' covering both prostatic lobes. With the development of benign prostatic hyperplasia (BPH) in the adult, the nerves are increasingly displaced laterally and anteriorly. Another finding of the study was that at the membranous urethra the nerve fibers are present all around the urethra between the 3 and the 9 o'clock positions and not only lateral to the urethra. These new anatomical insights have led to recent refinements in the technique of NS radical retropubic prostatectomy (RRP).

The laparoscopic and the robotic approaches to radical prostatectomy, unlike the conventional retrograde retropubic technique, are performed in an antigrade manner and anatomical details of the peculiar visualization of NVBs from the endoscopic perspective have been described by Tewari et al.[6,7] By combining cadaveric laparoscopic and open dissections, the authors have provided clear pictures and drawings showing key topographical details to guide the preservation of NVBs, such as the location of the pelvic plexus in relation to the seminal vesicles (when retrieved in an antigrade manner after dissection of the bladder neck) or the close vicinity of the cavernosal nerves to the lateral prostatic pedicles.

TECHNIQUES OF NEVER-SPARING SURGERY DURING RADICAL RETROPUBIC PROSTATECTOMY

Two main surgical approaches to an NSRRP have been described.[8] In the so-called 'anatomical technique', first reported by Walsh,[2,9,10] the nerve dissection is initiated at the apical level with primary isolation of the urethra. Ruckle and Zincke[11] have proposed an alternative technique where the neurovascular bundles are primarily dissected off the lateral prostate and only subsequently the urethra is transected. Several variants of this lateral approach to the neurovascular bundles have been subsequently described.[12–14]

The apical approach to the neurovascular bundle (the Walsh technique)[10]

There are a number of key steps in this technique that, if overlooked, may jeopardize the success of nerve preservation. For each of them, Walsh has provided useful tips to avoid inadvertent nerve injury during surgery. These are summarized below:

1. After division of the dorsal vein complex, the proximal vein edges on the anterior surface of the prostate need to be sutured in order to avoid back bleeding. This should be accomplished with a running V-shaped suture rather than trying to tie together the edges towards the midline. The latter maneuver may displace medially the bundles towards the anterior prostate, making their accurate dissection more difficult.
2. A critical point where the bundles may be damaged is during the transection of the urethra and the surrounding striated sphincter musculature. Because the neurovascular bundle when approaching the prostatic apex is located underneath the sphincter and can be fixated into a medial position by an apical vessel, care should be used to transect only the lateral edges of the sphincter at the urethral level, refraining from any dissection underneath the prostatic apex.
3. In order to avoid excessive traction while releasing the bundles from the lateral prostatic surface, after the urethra has been transected the catheter should be removed and the dissection carried out while the prostate is rolled from side to side.
4. By releasing the superficial layer of the lateral pelvic fascia, the prostate becomes more mobile and the neurovascular bundles move laterally. This maneuver is best accomplished by lifting up the prostatic fascia with a right-angle clamp starting at the bladder neck and proceeding down to the apex. At this point, a groove will appear on the posterolateral edge of the prostate as a landmark for the neurovascular bundle, which is located just laterally to it. Following the groove down to the apex will enable the identification of the bundles at the level of the transected urethra: only at this point can the dissection be completed at the apex and carried out posteriorly to develop the prostatic–rectal plane without damaging the nerves.
5. The bundles can now be released completely from the prostate with gentle

spreading of a right angle from the apex up to the midportion of the prostate. Some vessels that pierce the prostate at this level may prevent the release of the bundle and need to be divided with small hemoclips. Avoidance of unipolar electrocoagulation is of paramount importance for the maintenance of the integrity of the nerves.

6. The division of a small arterial vessel running from the neurovascular bundle, over the seminal vesicle to supply the prostatic base, usually enables the bundles to be completely freed from the prostate.
7. The last critical point for a successful nerve-sparing technique is represented by the dissection of the seminal vesicles. Because the midportion of the pelvic plexus is anatomically located at the tip of the seminal vesicles, the dissection of these small organs must be carried out very carefully, particularly in the lateral aspect, where small arterial branches are often encountered and need to be clipped close to the seminal vesicles.

The lateral approach to the neurovascular bundle

The Ruckle and Zincke technique[11]

This technique represents an alternative and simplified anatomical approach in which the dissection of the neurovascular bundles off the prostate precedes the apical dissection and the urethral transection. Briefly, after blunt perforation of the lateral prostatic fascia bilaterally, the dorsal vein complex is transected in between a double ligation with the creation of an oval defect in the dorsal prostatic fascia.[15] A vertical incision in the prostatic fascia is then conducted from one of the two lateral sides of the defect (for example the left) down to just above the left neurovascular bundle. From that point, the incision is extended superiorly towards the bladder and inferiorly towards the urethra parallel to the neurovascular bundle. Overall, the incision, if carried out in the left side, will appear as an upside down T to the operator positioned on the left side of the patient. By placing the index finger at the confluence of the incisions in the prostatic fascia, the left neurovascular bundle is swept laterally from the prostate. A posterior prostatic plane is then created by advancing the finger between the two layers of Denonvilliers' fascia: the anterior layer, attached to the posterior prostate, and the posterior one in contact with the rectum. The finger is further advanced until it reaches the lateral prostatic fascia of the controlateral right side. The fascia is then perforated and spread with a right-angle clamp medially to the right neurovascular bundle. This maneuver enables the right bundle to be freed from the prostate.

The Scardino technique[16,17]

In this technique, following the transection of the dorsal complex, the lateral pelvic fascia is incised medial to the neurovacular bundle on the anterolateral prostatic portion and the bundles are gently swept laterally from the prostate. A lateral retraction of the bundle allows Denonvilliers' fascia to be exposed. An incision is made on posterior Denonvilliers' fascia that covers the prerectal fat. Care must be taken to preserve Denonvilliers' fascia over the posterior prostate in order to reduce the risk of positive surgical margins.

The Klein and co-workers variant technique[12]

The authors describe their nerve-sparing technique as a modification of the initial dissection of the perirectal lateral pelvic fascia reported by Stephenson et al[18] in a non-nerve-sparing surgical approach of RRP. In a way conceptually similar to that of Ruckle and Zincke[11] and Scardino,[16,17] the incision of the lateral pelvic fascia along the longitudinal axis of the prostate begins at a level well medial to the neurovascular bundles. The bundles are then swept inferiorly and laterally from the prostate and then sharply dissected free from the prostate from apex to base. When the bundles have been completely freed on both sides, the plane between the posterior prostate and the anterior rectum is developed with blunt dissection rotating the prostate from side to side. Only at this point are the dorsal vein and the urethra divided.

The concept of 'curtain dissection' or 'high fascial incision technique'

Based on their anatomical findings of a 'curtain-shaped' disposition of the NVBs on the anterolateral surface of the prostatic lobes, Lunacek et al[5] propose to start the dissection of the prostatic fasciae anteriorly to preserve all the nerve fibers that are spread concavely in the 'curtain'. In a similar way, Montorsi et al[19] start the dissection of the NVBs by incising the prostatic fasciae at the 1 and 11 o'clock positions and direct the line of incision to the lateral border of the external urethral sphincter, thus allowing a displacement of the NVB at the level of the prostatic apex and the membranous urethra that is more efficient than in previous techniques.

TECHNIQUES OF NERVE-SPARING SURGERY DURING ENDOSCOPIC RADICAL PROSTATECTOMY

Since the introduction of endoscopic radical prostatectomy, several techniques for nerve preservation have been described for the laparoscopic and the robotic approach. These techniques, albeit initially developed with one of the two surgical methodologies, are in principle similar and applicable to both the laparoscopic and the robotic approach.

There are at least two controversial points of technique as regards the way to perform endoscopic nerve preservation. One concern is the dissection of the seminal vesicles, which can be carried out through the cul-de-sac between the bladder and the rectum[20,21] or by incising the bladder neck after exposure of the anterior surface of the bladder and the prostate base.[22] The pelvic plexus may be at more risk of transection, clipping, and coagulation during posterior dissection through the rectovesical cul-de-sac; at the same time, caution is also needed when approaching the seminal vesicles through incision of the posterior bladder neck as the pelvic plexus is located just lateral to the seminal vesicles.[6]

Controversy exists also as to whether the dissection of the NVBs should be carried out with an antegrade[6] or a retrograde approach.[23] Since the triangular space containing the NVBs is more prominent at the prostatic base rather than the apex, the antegrade approach can easily develop a plane of dissection within the triangle, leaving the medial fascia attached to the prostate. This dissection may not be easy in retrograde approaches of laparoscopic prostatectomies as the triangle is not so developed at the apex.[6]

Laparoscopic techniques of nerve-sparing radical prostatectomy

Both a retrograde and an antegrade technique of nerve preservation have been described for the laparoscopic approach. Rassweiler et al[23] reported a retrograde technique in which the periprostatic fascia was initially incised at the apex of the prostate and the NVB dissected off. Guillonneau and Vallancien[21] and Abbou et al[24] described making a 'lateral' incision in the periprostatic fascia after dividing the prostatic pedicles. Dissection of the NVB was then carried out from these lateral incisions.

While the above-mentioned techniques are conducted transperitoneally, Stolzenburg[25] has described an extraperitoneal approach to radical prostatectomy with nerve preservation.

More recently, the same author[26] has published a modified technique, named 'intrafascial NS endoscopic extraperitoneal RP', in which the procedure is initiated by dissecting the bladder neck at the 12 o'clock position without incising the endopelvic fascia as in the previous technique. A bilateral sharp incision of the periprostatic fascia is then conducted from the bladder neck down to the apex and the plane between the prostate and the fascia developed. Only at this point is the endopelvic fascia reflection over the prostate incised. The main goal of this approach is to develop the right plane and detach the prostate from its 'envelopment', leaving intact all lateral enveloping periprostatic fascia (including the endopelvic fascia) and puboprostatic ligaments as a continuous structure.

Robotic techniques of nerve-sparing radical prostatectomy

Techniques similar to the laparoscopic NSRP have been reported for the robotic NSRP.[27,28] Above all, the Vattikuti Institute prostatectomy with veil of Aphrodite nerve-sparing has gained popularity in view of its promising functional results.[29] Briefly, after division of the bladder neck at the prostatovesical junction, dissection of the seminal vesicles, and development of the plan between the posterior surface of the prostate and Denonvilliers' fascia, the two pillars of prostatic fascia appear clearly demarcated. The dissection of the veil of Aphrodite begins by entering the plane between the prostatic fascia and the capsule of the prostate, starting inferolaterally where the prostatic fascia reflects off the prostate, and proceeds in antegrade fashion. The prostatic pedicle is not ligated; rather, small arterioles are coagulated using bipolar coagulation as they enter the posterior surface of the prostate.

In order to eliminate the potential injurious effects of electrocautery on the NVBs, Ahlering et al[30] have achieved a cautery-free and clip-free preservation of the NVBs by placing laparoscopic bulldog clamps on the vascular pedicles although the functional benefits of this variant technique have not yet been reported.

DO THE DIFFERENT NERVE-SPARING TECHNIQUES DIFFER IN OUTCOMES?

The surgeon considering an NSRRP must balance the need for complete eradication of local tumor with the preservation of sexual function. A successful NS technique should combine a high probability of potency recovery with a low positive surgical margin (PSM) rate, particularly at the apex and the posterolateral prostate. Extensive literature has demonstrated that PSM adversely affects recurrence-free survival outcome after surgery.[31–34] A PSM is defined by the majority of authors as the extension of the tumor to the inked surface of the resected specimen and is considered an indicator of incomplete excision of the neoplasm.[35,36]

Because the cavernosal nerves cannot always be visualized on the dorsolateral prostate surface, Walsh[10] advises identifying them at the prostatourethral junction after dissecting the apex of the prostate. On the contrary, the supporters of the lateral approach to the bundles contend that identifying the nerves at the apex is more difficult.[11] Are these different approaches equally safe in terms of cancer control?

Ruckle and Zincke[11] compared 104 consecutive patients who had undergone the original Walsh nerve-sparing RRP before 1991 with 123 consecutive patients who had an NS procedure according to their modified technique after 1991. The PSM rate (32% in the Walsh technique vs 37% in the Ruckle and Zincke technique) did not significantly differ in the two groups. In a similar comparative study, Klein et al[12] reported a reduction in PSM from 33.3% to 15.5%, employing the Walsh technique, when their modified lateral approach to the bundles was used. However, these retrospective analyses are biased by potential confounds such us stage migration, improvement in preoperative selection criteria, and surgical expertise.

As far as sexual preservation, no study as yet has compared the degree of potency recovery among the different reported NS techniques. Outstanding postoperative potency rates varying from 86% to 62% have been reported employing the Walsh technique, but these seem to be confined only to centers of excellence.[37,38] The success rate of the procedure drops to 44% in a large retrospective survey of non-specialists[39] and falls to 21% in a single institutional prospective series assessing preoperative and postoperative outcomes with validated questionnaires.[40]

Improvements in surgical technique are expected to positively affect functional results, as recently shown in the study by Chuang et al,[41] where the overall potency rate increased from 40.5% when the NVBs were dissected off after division of the urethra, to 54.8% with early release of the NVBs, up to 66.1% when early release of NVBs was accomplished with 2.5× loop magnification.

The supporters of the endoscopic techniques of RP advocate the achievement of better preservation of NVBs as a result of improved magnification. Indeed excellent potency rates have been reported particularly with the robotic veil of Aphrodite technique[29] (see Table 11.2) and this might be related to an enhanced nerve sparing, as evidenced by the histological finding of reduced nerve bundles count and increased margin clearance in comparison with standard technique.[42]

Table 9.1 shows comparative potency rates and surgical margins with open retropubic and endoscopic RP series. The robotic approach seems to guarantee better functional results with no additional or even less price in terms of

Table 9.1 Comparative potency rates and surgical margins with open retropubic and endoscopic RP contamporary series

Series (first author)	*Technique*	*Number*	*Mean follow up (months)*	*PSM (%)*	*Intercourse rate at 1 year (%)*	*Patients with normal SHIM/ IIEF (%)*
Rabbani[43]	RRP	225	12	NA	42	8
Schover[44]	RRP	240	52	NA	NA	33
Chuang[41]	RRP	56	5.5	NA	66	NA
Guillonneau[45]	Laparoscopic	550	36	16.7	66	NA
Stolzenburg[46]	Laparoscopic	70	12	21	33	NA
Ahlering[47]	Robotic	60	9	17	33	NA
Bentas[48]	Robotic	40	15	30	22	NA
Menon[22]	Robotic	200	7.9	6	68	NA
Tewari[49]	Robotic	530	12	9	78	NA
Kaul[29]	Robotic	154	12	6.4	96	71
Chien[50]	Robotic	56	Minimum 3 months	10.7	–	66

Modified from Kaul et al,[29] with permission.
RRP, radical retropubic prostatectomy; PSM, positive surgical margin; NA, not applicable; SHIM, sexual health inventory for males; IIEF, international index of erectile function.

surgical margins. However, given the complex series of variables that can interfere with the success of a sexual sparing RRP, it has to be concluded that, out of a randomized prospective fashion, a comparison of potency outcomes for the different techniques of NSRRP may be an impossible task. No such study is at the moment available in the literature.

INDICATIONS FOR SPARING OR NOT SPARING THE NEUROVASCULAR BUNDLES

Preoperative indications

The majority of authors agrees that the ideal candidate for an NSRRP should be fully potent preoperatively and have an organ-confined cancer, i.e. a clinical T1/T2a and T2b disease.[35] Because the neurovascular bundles lie outside the capsule and fascia of the prostate, cancer control is not compromised by an NS procedure when the tumor is organ confined.

T1a and T1b are ideal for NS as they rarely invade the NVB.[51] T1c tumors have been reported to have a PSM rate varying from 0 to 59%,[52] so eligibility for an NS should be judged according to prostate-specific antigen (PSA) and Gleason score. T2a and T2b cancers with a contralateral negative biopsy are considered low-volume localized diseases with a high probability of being organ confined.[53] Low Gleason score[54] and PSA are preferable, since high preoperative PSA and biopsy grade increase the risk of extracapsular extension and therefore of PSM.[55,56] As shown in Table 9.2, a clinical T1 and T2 prostate cancer with a PSA <10 ng/ml and a Gleason score ≤7 constitute the main elegibility criteria for an NS procedure in the majority of authors. A useful tool to predict the probability of extracapsular tumor extension on the basis of preoperative parameters is represented by the Partin tables.[57] Cheng et al[58] found the combination of PSA value and the percentage of cancer in the biopsy specimen to accurately predict the risk for positive margins and proposed a model based on these two variables to select the candidates for NSRRP. Tigrani et al[59] studied 108 patients who underwent RP and found the number of positive biopsies and not PSA level, Gleason score, or primary grade to be the best predictor of margins status.

Others have advocated even more strict inclusion criteria. The neurovascular bundle located on the site of a positive biopsy that contains more than 50% of tumor or perineural invasion or a Gleason 7 or higher tumor should be removed according to Alsikafi and Brendler.[60]

Several authors have adopted the practice of sparing the nerve only on the site of a negative biopsy.[61–65] By doing so, Huland et al[64] found a 0% incidence of PSM on the nerve-sparing site, while 27% of patients had disease in the removed bundle. Similarly, Park et al[61] found a 32% rate of extracapsular extension on the site of positive biopsy vs only 7% when the biopsy was negative. The site-specific removal of the neurovascular bundle resulted in a potential reduction of positive surgical margins in 50% of patients with extracapsular extension. In the series of Graefen et al[63] the excision of the neurovascular bundle on the side of a positive biopsy excluded approximately 30% of patients from an NSRP unnecessarily, while the overall positive margin rate was 15.9%. The utility of using such strict selection criteria is also questioned by the observation that 78% of patients with unilateral positive biopsies have bilateral tumor involvement at the examination of the entire specimen.[53]

More recently, Naya et al[65] found that a prostate biopsy core specimen with a tumor length of at least 7 mm and a positive basal biopsy core specimen with any tumor length or grade were the best predictors of extraprostatic extension in the RP specimen. In a subsequent validation series, the presence of both criteria resulted in a 33% incidence of ipsilateral extraprostatic extension vs only 4.6% with neither criterion.

Table 9.2 Preoperative and intraoperative selection criteria for not performing a nerve-sparing procedure and the reported positive surgical margins rate

Criteria	*Sofer*[78]	*Walsh*[79]	*Alsikafi*[60]	*Graefen*[63]	*Scardino*[70]	*Shah*[80]
Preoperative selection criteria						
Clinical stage >T2	+	+	+	+	+	+
PSA >10 ng/ml	+					
GS = 7			+			
GS >7	+			+		
GS ≤6 if >50% tumor in biopsy[a]						+
GS = 7 if >30% tumor in biopsy[a]						+
GS ≥8–10 if >10% tumor in biopsy[a]						+
Partin tables		+			+	
Site of >50% tumor on biopsy[a]			+			
Site of perineural invasion[a]		±	+			+
Intraoperative selection criteria						
Site of palpable tumor[a]			+			
Site of positive biopsy[a]				+		
Induration of the lateral pelvic fascia[a]		+			+	
Adherence of the NVB to the prostate[a]		+			+	
Positive surgical margins	24%	5%	11%	15.9%	5%	8%

GS = Gleason score; PSA, prostate-specific antigen; NVB, neurovascular bundle.
[a]The NVB can be spared on the contralateral side.

When the absence of these criteria was prospectively used to guide nerve sparing, the incidence of an ipsilateral positive resection margin did not exceed 2.5%.[66]

Walsh[67] states that the site of a positive biopsy, or of a palpable tumor, or the presence of perineural invasion represent strict criteria upon which the decision to excise a neurovascular bundle should be based. A previous study showed that only 17% of patients with perineural invasion had a positive surgical margin at the level of the neurovascular bundle.[68] Similarly, in 452 consecutive patients undergoing RRP, perineural invasion detected on biopsy showed only a marginal association with positive surgical margins and bilateral nerve sparing on multivariate models.[69] Rather, a subjective intraoperative judgment is probably the most accurate indicator of the necessity to sacrifice the NVBs.[10]

Intraoperative indications

Walsh[10] recommends to proceed to secondary excision of the NVBs (which should always be spared in the first instance) in the presence of one of the following intraoperative findings:

1. induration in the lateral pelvic fascia
2. adherence of the NVB to the prostate while it is being released
3. inadequate tissue covering the posterolateral surface of the prostate once the prostate has been removed.

Other authors employ the same criteria as intraoperative indicators of wider dissection.[70] Alsikafi and Brendler[60] advocate wide excision of the neurovascular bundle(s) any time a tumor is palpable on one or both sides intraoperatively, particularly when at the apex. They describe the technique of transecting the anterior urethra 3 mm distal to the apex at all times.[60]

Some authors have addressed the question whether obtaining a frozen section of the apical soft tissue during an NSRRP may reduce the incidence of PSM at the prostatic apex, a site often involved by prostate cancer.[71] Shah et al[72] observed that the routine use of biopsy frozen section of apical soft tissue was responsible for achieving a disease-free status in only 2% of their patients. Other authors,[73] questioning the accuracy of preoperative assessment of the tumor extent by digital rectal examination[74] and a subjective intraoperative assessment of extracapsular extension,[75] decided to spare the bundles after obtaining intraoperative frozen sections in patients with prostate cancer at high risk of extracapsular extension. They reported a PSM rate of 26% and estimated the frozen sections enabled a 15% reduction of PSM. However, tumor was identified in only 20% of specimens, confirming the finding of previous studies where most patients with positive intraoperative frozen sections did not have detectable tumor in the removed NVB.[76] Frozen sections were used in 83 consecutive patients with intraoperative palpable lesion close to the capsule to guide for nerve-sparing surgery. The presence of carcinoma adherent to the capsule resulted in a twofold incidence of pathological T3 tumor compared with the control group (intraoperatively non-palpable lesion) and 14% of carcinoma invasion in the resected NVBs.[77]

Table 9.2 lists the indications criteria adopted in some high-volume institutions to decide whether or not to spare the neurovascular bundle(s). The PSM rates should not be taken as an absolute indicator of the validity of the reported criteria since they may be largely influenced by the surgical ability.

DOES NERVE-SPARING SURGERY AFFECT THE RISK OF POSITIVE SURGICAL MARGINS?

Since the surgical boundaries are reduced by performing an NS procedure, this may result in a higher rate of positive surgical margins, particularly in the posterolateral prostate. The region of the neurovascular bundle has been shown to be the most common site of capsular penetration.[18,81] Using the NS procedure, Catalona and Bigg[82] reported that all patients with extracapsular extension in the region of the neurovascular bundle had positive surgical margins.

In spite of these premises, it is a fact that, irrespective of the widespread use of an NS approach, the overall rate of positive surgical margins has continuously declined over the last two decades.[35] A shift in the prostate cancer population towards an intracapsular disease, together with refinements in surgical technique[83] and improvement in surgical expertise,[84] are the most likely explanations. In the presence of these confounds, it has become difficult to interpret the potential negative impact of NS procedures.

A few studies have addressed the question whether NSRRP patients may have an increased risk of positive surgical margins. The group of Scardino[36,85] documented a further decrease in positive surgical margins from 19% in 1989 to 8% in 1993 in spite of the introduction of their lateral approach to the neurovascular bundle. Similarly, earlier reports failed to demonstrate a statistically significant difference in the rate of positive margins between NS and non-NSRRP.[86–88] Overall, positive surgical margin rate was 24% in NS patients and 31% in non-nerve-sparing (non-NS) patients in the series of Sofer.[78] The two groups of patients were also equally distributed as regards the incidence of posterolateral margins. Even after adjusting the patients for the major potential prognostic factors, the NS status did seem to affect cancer control. In the light of these results, several authors nowadays believe that in appropriately selected patients the NS approach does not compromise cancer control and that no more than 7% of positive surgical margins can be attributed to nerve preservation.[89,90] In the most recent series by Walsh[79] of 500 consecutive patients in which the NVB was widely excised only on one side in 13% of cases, the overall PSM rate was 5%.

Recently, a large multicentric retrospective review of 9035 RPs performed in the last 20 years found the overall positive surgical margin rate falling from 40% between 1982 and 1986 to 10% between 1997 and 2002. However, the positive surgical margin rate in the pT3 disease population slightly increased between 1997 and 2002, implying that the decrease in surgical margin rates is most likely due to stage migration rather than major improvement in surgical technique.[91] Because patients, particularly the pT3 group, were not stratified according to nerve preservation, the potential negative impact of the NS technique remains to be elucidated.

When present, an extensive capsular perforation has been reported to occur in the region of the neurovascular bundles in 87% of cases, resulting in 57% of positive surgical margins.[85] Negative surgical margins were achieved in 58% of cases after wide excision of the bundles, compared with a 45% rate when both bundles were left intact in a series of 107 patients with posterolateral extensive capsular perforation. Long-term follow-up showed a sustained improvement in disease-free survival for the negative margin patients.[92] Park[61] introduced the concept of the ratio between the positive surgical margin (PSM) rate and the extracapsular extension (ECE) rate to assess the benefit of excising the neurovascular bundle. He found that in series employing more liberal indications for NS, the PSM/ECE ratio was higher[90] than in those using more conservative NS approaches (68 vs 50).[53,93]

A positive surgical margin may also be the result of cutting through inside the glandular area of the prostate.[94] An NS procedure is expected to carry a higher risk of these ‘intraprostatic surgical margins’. Based on the histological review of a large series of NSRRP patients, inadvertent capsular incision during surgery had occurred in no more 2.3% of cases.[95] Even if these figures are too optimistic, literature data have shown intraprostatic surgical margins have little or no effect on oncological outcome.[85,96] When nerve-sparing surgery was included as a variable in a multivariate analysis in combination with established risk factors using biochemical failure as endpoint, it did not affect the oncological outcome in a large series of 1343 RPs. In addition, positive surgical margins in pT2 cancers were remarkably similar (6.5 vs 5.1%) in the NS and non-NS groups.[97]

These studies, taken together, suggest that NSRRP nowadays does not seem to have a significant impact on prostate cancer control, as the majority of patients elected for surgery have an organ-confined disease. Continuous improvement in diagnostic criteria will probably help to better identify those patients with extracapsular extension for whom the preservation of bundles may translate into positive surgical margins.

CONCLUSIONS

The technique of sparing the erigentes nerves during radical prostatectomy was described more than 20 years ago for RRP. This operation is currently routinely performed worldwide but excellent results, particularly for potency preservation, seem to be confined to a few centers of excellence. The improvement in cancer control, demonstrated by a slight but continuous reduction of the PSM rate over the years, has not been accompanied by a similar increase in potency preservation. There is even the suspicion that the better oncological results may simply reflect a stage migration and not an amelioration of the surgical technique.

Endoscopic techniques have so far produced results at least comparable to open surgery. Notably, some of the latest robotic RP series have reported astonishing potency preservation rates, approaching 90%, together with a dramatically low incidence of positive surgical margins. Will these results remain confined to centers of excellence (as occurred for RRP) or become routine standard? If the former turns out be the case, some may even dare to ponder whether the future of prostate cancer cure should be surgical at all.

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CHAPTER 10

Non-nerve-sparing radical prostatectomy

Gregory P Zagaja and Charles B Brendler

INTRODUCTION

Radical retropubic prostatectomy (RRP) provides excellent cancer control in most patients with clinically localized prostate cancer. However, locally recurrent disease and/or distant metastasis will develop in approximately 30% of men with clinically localized prostate cancer by 10 years following radical prostatectomy (RP). The risk of disease recurrence significantly increases with extracapsular extension (ECE) and positive surgical margins (PSMs). Between 27% and 53% of men with PSMs will have biochemical progression within 10 years after surgery.[1–3] Most recurrences occur within the first 2 years,[4] while up to 20% occur beyond 5 years.[2] Additionally, it is estimated that 35% of patients experiencing biochemical failure will subsequently develop clinically recurrent disease requiring adjuvant therapy.[5]

Although somewhat controversial, surgical margin status is generally recognized to be an independent risk factor for recurrence after RRP, and it is the only factor that can be modified by surgical technique.[6] Although the incidence of a PSM after RRP has declined in the last 15 years,[7] most likely due to stage migration, PSM rates still vary widely, with one recent series reporting a PSM rate of 37%.[8] To achieve a surgical cure in the presence of extracapsular disease, a sufficiently wide excision of periprostatic tissue is necessary to yield negative surgical margins. Most series reporting a significant decrease in PSM rates are from academic institutions[6,7] in which large volumes of cases are performed. Thus, it seems that experience and careful attention to surgical technique play a significant role in decreasing the incidence of PSM. We have made several modifications in the technique of anatomical radical prostatectomy, particularly regarding wide excision of periprostatic tissue in individuals with advanced grade and stage of disease. Herein we present our indications for wide excision of the neurovascular bundle (NVB), modifications in the surgical technique as previously described[9,10] and our outcomes with regard to PSMs and its impact on biochemical disease-free survival.

INDICATIONS FOR ALTERED SURGICAL APPROACH

Several multivariate statistical models have been proposed to estimate pathological stage at RP with the intent of facilitating intraoperative decision making. Of these methods, the Partin tables represent the most widely used example, in which clinical stage, pretreatment prostate-specific antigen (PSA), and Gleason grade on prostate biopsy are used to predict pathological stage at RP.[11] We have developed criteria by which patients unsuitable for nerve-sparing prostatectomy may be identified based on an increased potential for having ECE and PSMs. There are relatively few absolute contraindications to NVB preservation, but, rather, each individual case should be evaluated based on these clinical prognostic factors before a decision can be made to proceed with nerve preservation. Nomograms currently exist to assist in determining the risk and side of ECE in high-risk patients.[12,13] Our indications for wide excision of the NVBs are as follows:

Absolute indications

- Locally advanced disease (T3)
- Palpable disease at the apex
- Gleason grade 5 disease
- Serum PSA ≥20 ng/ml
- Preoperative impotence.

Relative indications

- Intraoperative difficulties with mobilization of the NVB
- Intraoperative detection of a palpable nodule at the apex or along the NVB
- Serum PSA >10 and <20 ng/ml
- Greater than 50% Gleason grade 4 on biopsy
- Perineural invasion on biopsy
- Cancer present in three or more biopsy cores from the same lobe.

SURGICAL MODIFICATIONS

Identification of prostatourethral junction

In order to best visualize the prostatourethral junction, the levator ani muscle investing the apex of the prostate and membranous urethra should be dissected laterally. This is accomplished by a combination of sharp and blunt dissection using a Kittner dissector. It is then possible to visualize and palpate the prostatourethral junction and determine how much of the puboprostatic ligaments needs to be divided to facilitate division of the dorsal venous complex (DVC) of the penis. The puboprostatic ligaments are divided only as far caudally as is necessary to divide the DVC beyond the prostatic apex. The puboprostatic ligaments are divided sharply and not avulsed by blunt finger dissection, which may compromise the anterior support of the membranous urethra and impair subsequent urinary control. Although controversy exists about the anatomy of the puboprostatic ligaments,[14,15] there is little doubt that these ligaments tether the proximal membranous urethra and apex of the prostate to the undersurface of the symphysis pubis, which obscures the apex of the prostate. We believe it is essential to divide the prostatic portion of these ligaments to expose the prostatourethral junction, while attempting to preserve as much anterior urethral support as possible (Figure 10.1).

Transection of the dorsal venous complex

The dorsal venous complex of the penis is transected 10–15 mm distal to the prostatourethral junction. The DVC must be divided distal to the apex of the prostate to avoid apical injury to the prostate. Once the DVC is divided, it is then oversewn in a running fashion with a 2-0 polyglactin suture to ensure complete hemostatic control (Figure 10.2). When oversewing the DVC, care should be taken to suture only the complex and not incorporate the urethra or muscle fibers of the striated sphincter; injury to either may compromise urinary control.

Division of the membranous urethra

After the DVC has been hemostatically controlled, the anterior urethra is divided. In patients with

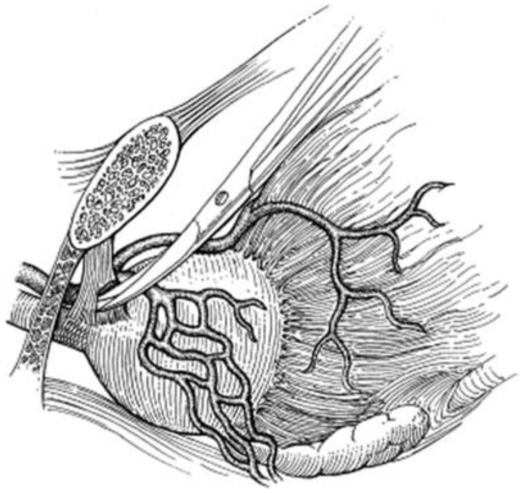

Figure 10.1 Partial transection of the puboprostatic ligaments after dissection of the levator ani muscle laterally from the apex and membranous urethra to precisely identify the prostatic urethral junction. (Reproduced from Kuznetsov DD, Alsikafi NF, Brendler CB. Surgical tips to help preserve urinary continence after radical retropubic prostatectomy. Contemporary urology, October 2001, with permission.)

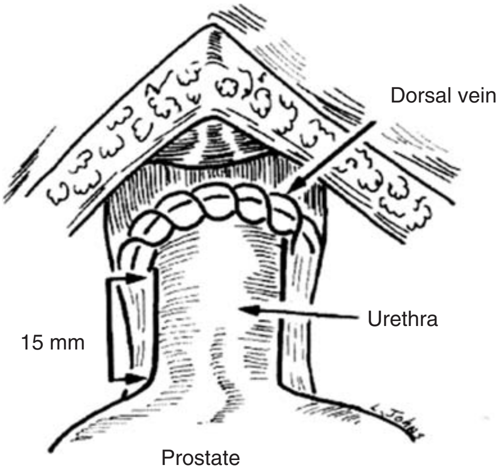

Figure 10.2 Transection and oversewing of the dorsal vein of the penis 15 mm beyond the prostatic apex allows for excellent exposure of the membranous urethra.

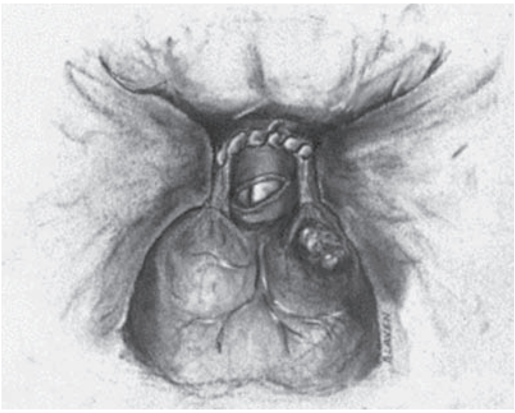

Figure 10.3 Oblique transection of the membranous urethra to avoid tumor at the apex of the right lobe.

clinical stage T1C disease, the membranous urethra can be divided immediately distal to the apex of the prostate. In patients with palpable disease, particularly at the apex, it is often necessary to modify the ipsilateral urethral dissection and remove 1–3 mm of membranous urethra to obtain a negative surgical margin (Figure 10.3). The urethra is divided sharply with the investing periurethral tissue and transected 180 degrees until the remaining urethra forms a horizontal plate with the underlying striated urethral sphincter.

Division of the prostatic ischial ligaments (prostatic pillars)

In patients with palpable disease at the apex, the ipsilateral prostatic ischial ligament (or prostatic pillar), which attaches the prostate caudally to the urogenital diaphragm, should be divided at the level of the urogenital diaphragm before dividing the posterior membranous urethra (Figure 10.4A). The urethral catheter is then removed to clearly expose the posterior urethra and underlying striated urethral sphincter. If, instead, the catheter is divided and traction placed on the prostate, the posterior lip

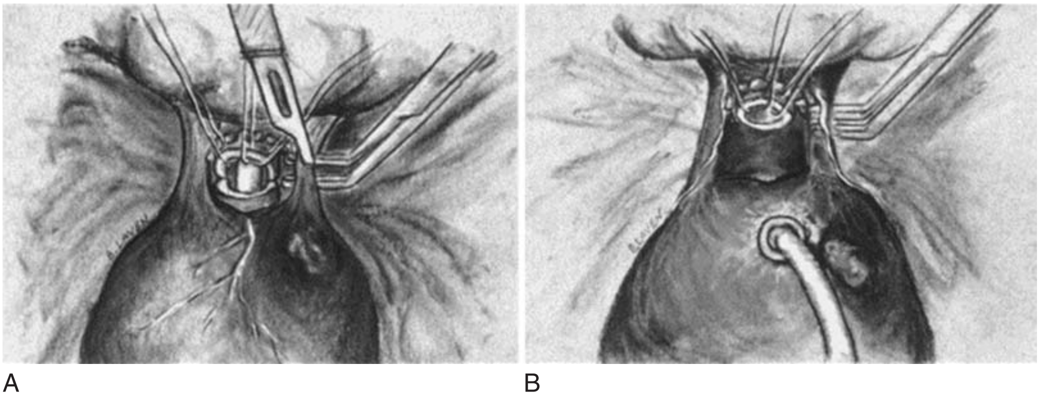

Figure 10.4 (A) Transection of the right prostatic pillar at the level of the urogenital diaphragm. (B) Transection of the right NVB at the level of the membraneous urethra before mobilization of the prosate from rectum.

of the prostate may be inadvertently entered when incising the posterior urethra. A long right-angled McDougal clamp is inserted under the striated urethral sphincter and posterior aspect of the urethra, and these structures are divided with a No. 15 scalpel blade. No attempt is made to separate the posterior aspect of the urethra from the underlying striated urethral sphincter because division of these two structures en bloc facilitates incorporation of both structures into the subsequent vesicourethral anastomosis, which we believe contributes to postoperative urinary continence. When dividing this tissue, once again, care is taken not to injure the posterior lip of the prostate which frequently lies close to the line of transection and sometimes may extend further distal. It is, therefore, imperative that this portion of the procedure be performed with good hemostasis and under direct vision. The utilization of surgical loupes during the extirpative portion of the procedure may optimize cancer control, while helping to preserve urinary control and potency.

Division of the neurovascular bundles

After dividing the urethra, the NVB is ligated with a hemoclip and divided at the level of the urogenital diaphragm before mobilizing the prostate from the rectum (Figure 12.4B). If the prostate is mobilized from the rectum prior to division of the NVB, the NVB and/or prostatic apical tissue may be avulsed, potentially compromising the soft tissue margins around the apex of the prostate. Once the NVB has been transected, the prostate is freed from the anterior rectal wall under direct vision. When the NVB is to be excised, dissection continues laterally after division of the rectourethralis muscle, which permits removal of a wide margin of the NVB and adjacent soft tissue with the prostate. This is accomplished utilizing a right-angle clamp and large right-angle clips (Figure 10.5A). The lateral pelvic fascia overlying the prostate is not incised but divided widely with the underlying neurovascular bundle. This process allows for excellent hemostasis and wider surgical margins around the tumor.

Adherence of the NVB to the prostatic fascia during their mobilization may indicate tumor involvement. This adherence may represent a desmoplastic reaction to tumor or a more benign process such as post-biopsy inflammation, prostatitis, or benign prostatic hyperplasia (BPH). In the presence of induration detected in the region of the neurovascular bundles, particularly

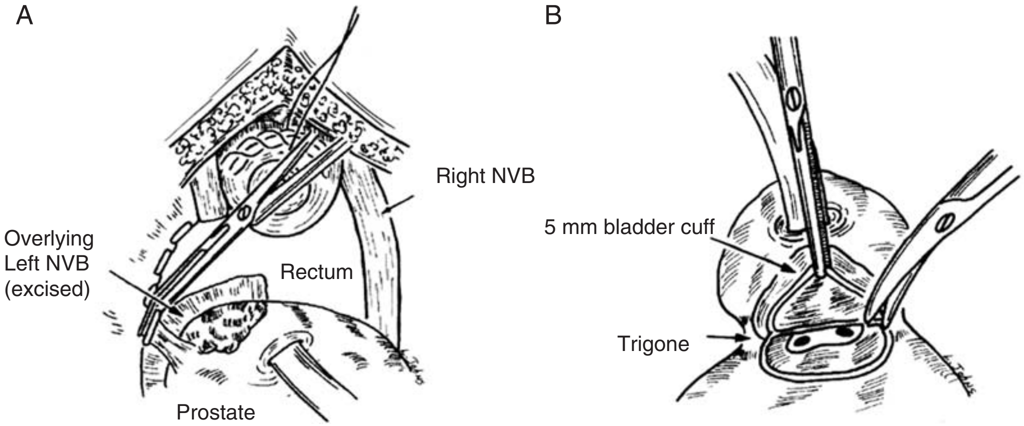

Figure 10.5 (A) Wide excision of the left NVB using clips for hemostasis. (B) Excision of 5 mm cuff of bladder tissue with the prostate when transecting the bladder neck.

when the bundles are adherent to the prostatic fascia, wide excision of the ipsilateral NVB should be performed. If an attempt is made to preserve the bundle in this setting, an intraoperative frozen section of the inked surgical margin should be obtained. If tumor is identified at the surgical margin, a subsequent wide excision of the ipsilateral neurovascular bundle is performed from the urogenital diaphragm cephalad to the inferior vesicle pedicle.

Dissection of the prostate from the anterior rectal wall

After the striated urethral sphincter and urethra have been divided, a few fibers of the rectourethralis muscle remain to be divided. Others have recommended that these fibers be divided by blunt finger dissection to free the prostate from the rectum. We believe that this dissection should be performed sharply, because blunt dissection may potentially avulse a piece of prostate, compromising the posterior surgical margin. Additionally, sharp dissection under direct vision decreases the potential risk of rectal injury. Once the striated urethral sphincter has been divided, a right-angle clamp is inserted beneath the fibers of the rectourethralis musle and these fibers are divided carefully until the entire posterior surface of the prostate is completely freed from the rectum.

Bladder neck dissection

Once the prostate is fully mobilized laterally and posteriorly, the bladder is opened anteriorly. Although the bladder neck is an infrequent site of positive surgical margins, they may occur there, particularly in those patients with tumors at the base of the prostate. Since bladder neck preservation has not been shown to improve urinary continence, we believe that a 5 mm cuff of bladder tissue should be removed circumferentially with the prostate (Figure 10.5B). The bladder neck should then be reconstructed prior to the vesicourethral anastomosis.

OUTCOMES ANALYSIS

Recently we reported the impact of these surgical modifications on surgical margin status and long-term cancer control.[14] A cohort of 996 consecutive patients who underwent RRP for clinically localized prostate cancer (clinical stage T1b–T2 disease) by a single surgeon (C.B.B.) was reviewed. Mean age was 60.1 years (range 41–77). All prostate specimens were inked and then fixed in buffered zinc formalin. The apical margin was sectioned transversely in 1 mm sections and then sectioned longitudinally to allow precise examination of the apical margin. The remainder of the prostate was serially sectioned transversally at 3 mm intervals. Tumor present at ink was noted as a positive surgical margin, which was defined as focal when there was a solitary positive margin and extensive when the positive margin was multifocal. Patients with extension of tumor through the capsule were considered to have ECE. Seminal vesicle invasion was defined as tumor invasion through the perivesicular fascia. All tumors were graded by the Gleason system and all lymph nodes sent for pathological analysis were examined carefully for metastatic disease. Patients were assessed at regular interval following RRP. Biochemical recurrence (BR) was defined as a PSA ≥0.1 ng/ml.

RESULTS

Baseline demographics data are presented in Table 12.1. About 60% of the patients had T1c disease and 40% had T2 disease. Overall, close to 92% of all patients had a moderately differentiated tumor (Gleason sum 5–7) on preoperative biopsy (93.7%, 86.8%, and 87.1% of the T1c, T2a, and T2b patients, respectively).

The overall PSM rate was 88/996 (8.8%). Only 12/694 (1.7%) patients with organ-confined (OC) disease had a PSM. In patients with extraprostatic extension, 60/241 (24.9%) and 16/59 (27.1%) patients with pT3a and pT3b disease had a PSM, respectively. The incidence of PSM increased significantly with both clinical stage and pathological stage. There was also a statistically significant correlation between PSM and higher postoperative Gleason score (Table 10.2).

Table 10.1 Baseline demographics

No. of patients	996
No. of patients with follow-up	968/996 (97.2%)
Mean age	60.1 ± 6.9 years (range 41–77)
Mean preop PSA (ng/ml)	7.4 ± 5.4 (0.4–53)
Clinical stage:	
• T1b	4 (0.4%)
• T1c	602 (60.4%)
• T2a	196 (19.7%)
• T2b	194 (19.5%)
Preop Gleason score:[a]	
• 3–4	36 (3.7%)
• 5–6	709 (71.9%)
• 7	201 (20.4%)
• 8–10	40 (4.0%)

[a] Gleason score information missing in 10 patients.
PSA, prostate-specific antigen.

Using a univariate logistic regression model, we found that, following the introduction of surgical modifications in 1995 and again in 1999,[9,10] there was a steady decrease in the PSM rate (Figure 10.6A). Of note, when the study group was analyzed by pathological stage, a strongly significant decrease in PSM rates over time was found in patients with ECE (Figure 10.6B). This also held true in patients with OC disease (Figure 10.6C), although the decrease in PSM was less pronounced.

In assessing biochemical progression, 968/996 (97.2%) patients were available for follow-up. Mean follow-up was 6.4 years. A total of 98 patients (10.1%) developed BR. Within this group, 36.7% of the patients progressed within 1 year after surgery and 61.2% within the first 2 years; only 12 (12.2%) patients progressed after 5 years postoperatively. Mean time to recurrence was 2.4 years (range 0.1–9.4). Of the 968 patients available for follow-up, 871 (90%) and

Table 10.2 Clinicopathological stage and surgical margin status

Clinical		pT2		PSM		pT3a		PSM		pT3b		PSM		Overall PSM	
stage	*No.*	*No.*	*(%)*	*No.*	*(%)*	*No.*	*(%)*	*No.*	*(%)*	*No.*	*(%)*	*No.*	*(%)*	*No.*	*(%)*
cT1b	4	3	(75)	0	(0)	1	(25)	1	(100)	–	–	–	–	1	(25)
cT1c	602	480	(79.7)	7	(1.5)	103	(17.1)	31	(30.1)	17	(2.8)	6	(35.3)	44	(7.3)
cT2a	196	130	(66.3)	3	(2.3)	57	(29.1)	10	(17.5)	9	(4.6)	1	(11.1)	14	(7.1)
cT2b	194	81	(41.8)	2	(2.5)	80	(41.2)	18	(22.5)	33	(17.0)	10	(30.3)	29	(14.9)
Total	996[a]	694	(69.7)	12	(1.7)	241	(24.2)	60	(24.9)	59	(5.9)	17	(27.1)	88	(8.8)

PSM, position surgical margin.

[a] 2 patients pT0.

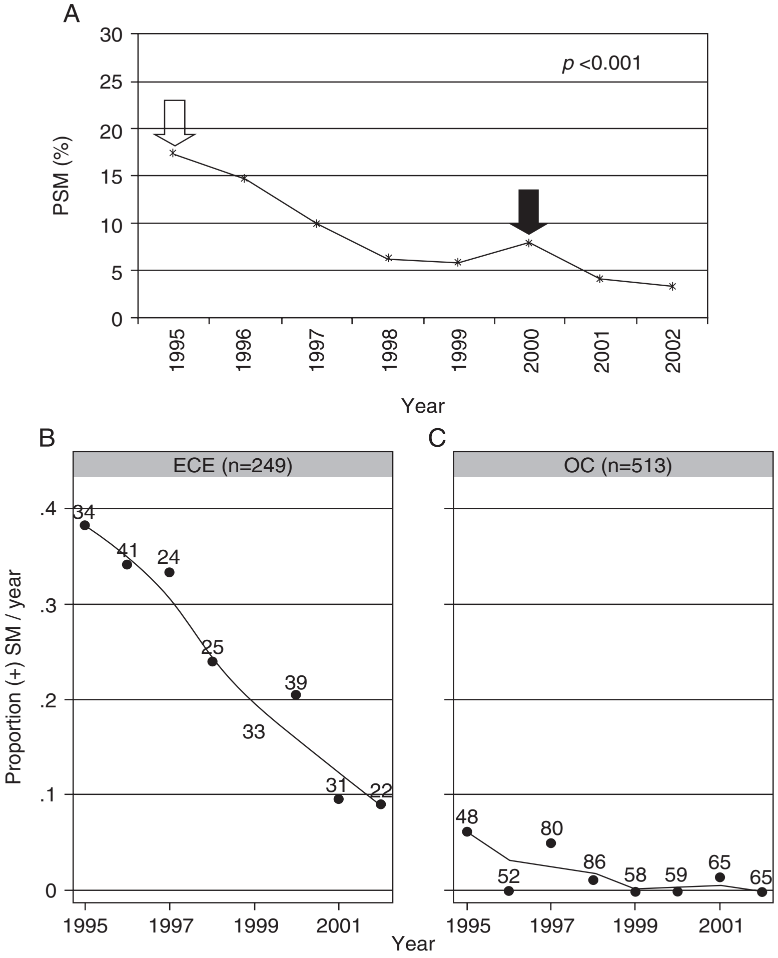

Figure 10.6 Trends in surgical margin (SM) status and pathological stage 1995–2002. (A) Surgical modification introduced in 1995[9] white arrow and in 2000[10] black arrow. (B and C) Decreasing trend in the proportion of (+) SM in the ECE and OC groups. Total number of procedures performed is indicated for each year. The trend line is based on the Lowess smoothing fit of the data.[17]

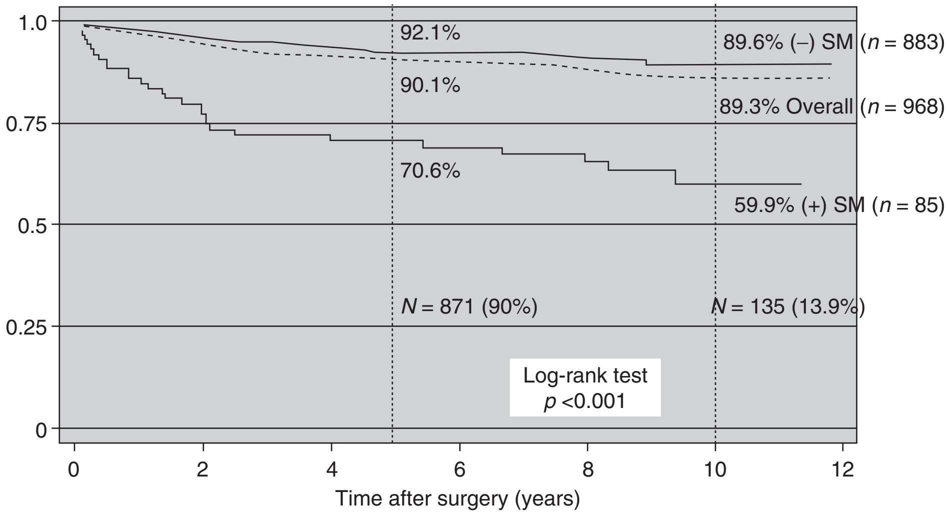

Figure 10.7 Biochemical disease-free survival, overall and by surgical margin status.

135 (13.9%) had at least 5- and 10-year follow-up, respectively. Kaplan–Meier analysis demonstrated actuarial 5- and 10-year biochemical disease-free survival rates of 90.1% and 86.3%, respectively (Figure 10.7). Overall, only 89/968 (9.2%) patients received some form of adjuvant therapy after RRP. Nine (9.2%) men died from prostate cancer, which accounted for 0.9% of the total population. Actuarial cancer specific survival rates were 99.7% and 97.8% at 5 and 10 years, respectively.

In assessing biochemical progression as a function of surgical margin status, 69/883 (7.8%) patients with negative surgical margins developed biochemical progression compared to 29/85 (34%) of those with PSM (p <0.001). Patients with negative surgical margins had actuarial 5- and 10-year biochemical disease-free survival estimates of 92.1% and 89.6%, respectively. In contrast, in patients with PSM, actuarial 5- and 10-year biochemical disease-free survival rates were 70.6% and 59.9%, respectively (p <0.0001) (see Figure 10.7). The presence of a PSM was a significant predictor of recurrence in patients with both organ-confined and pT3a disease (p <0.0001 and p = 0.011, respectively). Conversely, the risk of BR within the pT3b population was not affected by the presence of a PSM (Figure 10.8).

Log-rank tests comparing biochemical disease-free survival estimates across preoperative PSA, clinical stage, pathological stage, and final pathological Gleason score were obtained. All variables were strongly significant predictors of biochemical progression on univariate analysis (p <0.001), except for preoperative PSA, which did not quite reach significance (p = 0.07) (Table 10.3).

As shown in Table 10.4, on multivariate analysis, the presence of a PSM and both final pathological stage and Gleason grade were the strongest predictors of subsequent BR (p <0.001). Clinical stage T2b and ECE (pT3a/b) disease were also significant predictors of BR.

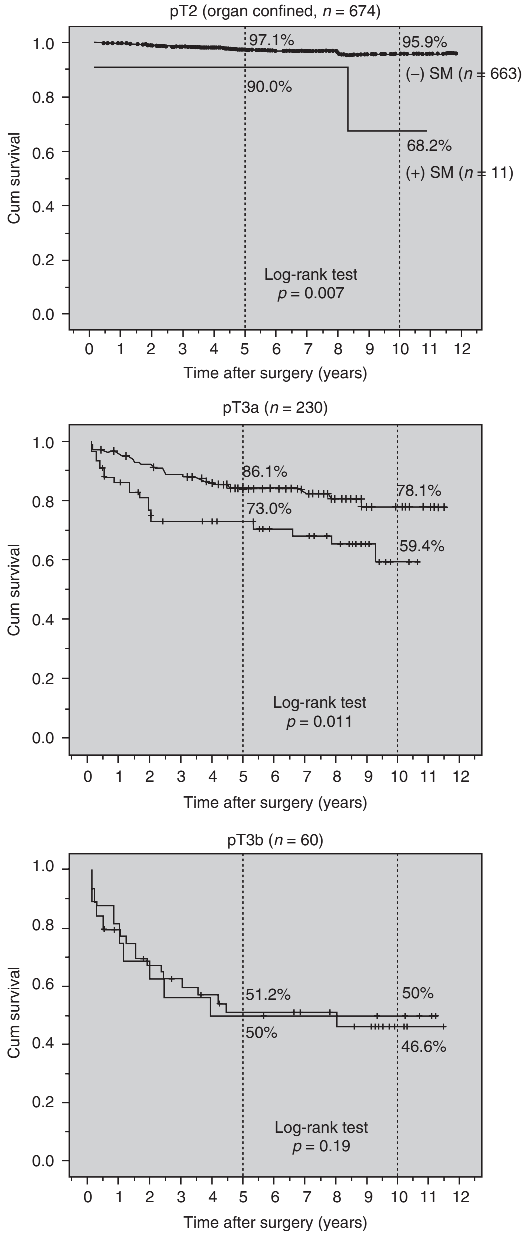

Figure 10.8 Biochemical disease-free survival by surgical margin and pathological stage.

Table 10.3 Log-rank test univeriate analysis to predict biochemical disease progression

Parameter	*p value*
Preoperative PSA	0.07
PSM	<0.0001
Clinical stage	<0.0001
Pathological stage	<0.0001
Final pathological Gleason grade	<0.001

PSA, prostate-specific antigen; PSM, positive surgical margin.

Preoperative PSA and clinical stage T1c and T2a disease were not found to be significantly associated with recurrence. After adjusting for preoperative PSA, clinical stage, pathological stage, and postoperative Gleason sum, the presence of a PSM was still strongly associated with a higher probability of BR (p <0.001).

Table 10.4 Cox multivariate proportional hazards to predict biochemical disease progression

Parameter	*HR*	*p value*	*95% CI*
Preoperative PSA	1.01	0.26	0.98–1.1
PSM	3.27	<0.001	2.1–5.1
Clinical stage:			
• T2a	1.73	0.06	0.99–3.0
• T2b	1.99	0.008	1.2–3.3
Pathological stage:			
• T3a	3.64	<0.001	2.1–6.3
• T3b	6.53	<0.001	3.4–12.3
Final pathological Gleason grade			
• 7	7.2	<0.001	3.9–12.9
• 8–10	21.0	<0.001	10.2–43.4

HR = hazard ratio; PSA, prostate-specific antigen; PSM, positive surgical margin.

SUMMARY

Surgical margin status is an independent risk factor for recurrence after RRP and is the only factor that can be modified by surgical technique. The surgical modifications which we have described have led to significantly decreased PSM rates. The presence of a PSM is a significant predictor of biochemical recurrence. A reduction in the rate of positive surgical margins has led to increased long-term cancer control. We contend that a strict adherence to surgical technique, particularly in individuals with high-risk disease, will result in lower PSM rates, lower BR rates, and hence a greater likelihood for long-term disease-free survival.

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CHAPTER 11

Nerve grafting

Joseph A Pettus and Farhang Rabbani

INTRODUCTION

The advent of widespread prostate-specific antigen (PSA) testing has led to considerable stage migration in prostate cancer. Contemporary patients are more often diagnosed with clinically localized, moderately differentiated prostate tumors than in the past.[1,2] Nevertheless, a substantial minority of patients present with locally advanced or high-grade tumors which may require more aggressive surgery to ensure oncological efficacy.

Successful radical prostatectomy (RP) strives to optimize three competing goals: extirpation of the tumor with clear margins, minimizing damage to the continence mechanism, and preservation of potency. The anatomical radical prostatectomy operation has undergone numerous refinements aimed at balancing these opposing interests since being first described by Walsh.[3,4] Still, recent data show that even in large volume centers, only 60% of patients are cancer-free, continent, and potent 2 years following contemporary radical prostatectomy.[5]

Potency following RP is mainly due to avoidance of neurovascular injury to the cavernous nerves.[3,4,6,7] The cavernous nerve fibers arise from S2–S4 of the spinal cord and travel within the pelvic plexus, then coalescing within the neurovascular bundle located posterolateral to the prostate in the groove between the rectum and prostate and finally reaching the corpora cavernosa distal to the prostatic apex. In the setting of high-grade or posterolaterally located tumors, resection of the neurovascular bundle is sometimes necessary to optimize cancer control and achieve negative surgical margins. Return of potency is directly related to the number of cavernous nerve fibers preserved at surgery.[7] Large series report 21–56% return of potency in patients who have had one nerve bundle resected compared to 55–76% in those with both nerves preserved.[7–9] Wide resection of both nerves essentially guarantees no erectile function postoperatively.[10,11]

Quinlan and colleagues were first to perform genitofemoral nerve grafting in rats following bilateral ablation of the carvernous nerves.[12] They observed superior erectile function in the nerve-grafted rats compared with sham-treated controls by 4 months. In 1999, Kim et al reported that 2/9 patients treated with bilateral cavernous nerve grafts had erectile function sufficient for intercourse.[13] That group subsequently reported that 10/23 (43%) patients with at least 1-year follow up had erections adequate for penetration using sildenafil.[10] They further noted that functional return did not occur until at least 5 months postoperatively and reached a plateau at 18 months. These early reports of success form the basis for subsequent studies of cavernous nerve grafting.

RATIONALE

Nerve regeneration is a complex, highly orchestrated process.[14] Within hours of peripheral nerve injury, the distal end undergoes Wallerian degeneration, characterized by demyelination, and cell membrane degeneration and leakage of various neurotrophic factors with subsequent phagocytosis by macrophages. The proximal nerve stump retracts to the level of the most proximal node of Ranvier and starts to sprout axons.[15] Within 3 days of axotomy, the distal axonal membrane and surrounding Schwann cells are phagocytosed by macrophages. The macrophages and other surrounding cells elaborate cytokines and neurotrophic factors that stimulate Schwann cells to proliferate. Over the course of days and weeks, the new Schwann cells form conduits for the regenerating axons and provide neurotrophic stimuli, allowing for appropriate dendritic connections to be made and ultimately, reinnervation of the end organ.[16–18] In the absence of Schwann cell stimuli, regenerating axons may grow inappropriately and fail to reinnervate the end organ. Axonal regeneration is slow, occurring at only 1–2 mm/day, and end-organ reinnervation is inversely proportional to the distance of regeneration. A nerve graft also experiences the same phagocytosis and Schwann cell proliferation, which act as a guide for axonal regeneration by providing physical structural support and a conducive microenvironment.

In animal models, researchers have demonstrated a variety of techniques which facilitate nerve regrowth. Quinlan[12] was first to apply genitofemoral nerve grafts to the cavernous nerves in a rat model. That group performed 3 mm cavernous nerve ablations bilaterally, and compared nerve-grafted rats to those without nerve grafts. The grafted rats had significantly better erectile function at 4 months, with 50% of grafted rats having functional return compared with 11% of the control rats after electrostimulation. Burgers and colleagues[19] applied nerve growth factor (NGF) locally to rats with 3 mm bilateral cavernous nerve grafts, comparing them with bilaterally grafted rats without NGF. They observed that 64% of grafted rats with NGF had erectile function compared with 33% of rats with grafts alone. Cavernous nerve regeneration has also been demonstrated using Silastic tube grafts;[20] May et al[21] recently reported that Silastic conduits lined with cultured Schwann cells restored erectile function comparable to sham controls.

The rodent model has several shortcomings. Rats are known to have excellent nerve regenerative capacity, the cavernous nerve is a more distinct entity than in humans, and the ability to create a large gap is limited. The canine cavernous nerve anatomy is more similar to that of humans. In dogs, the cavernous nerve is a plexus, rather than a distinct structure, containing both myelinated and unmyelinated fibers. Lowe and colleagues[22] recently performed 3 cm bilateral cavernous nerve ablation in dogs and compared bilaterally grafted to ungrafted dogs. They reported that grafted dogs had return of preoperative erectile function by 4 months and that the ablated animals still had significant deficits by 8 months. Further, histological examination of the grafts at 8 months demonstrated evidence of regeneration in the mid and distal segments of the graft with minimal Wallerian degeneration in the distal cavernous nerve stump. Return of parasympathetic function has been demonstrated in humans with phrenic nerve grafts for vocal cords[23] and in cardiac transplantation.[24] Even though the sural and genitofemoral grafts are myelinated, they undergo the same degeneration as described above, leaving proliferating Schwann cells whose basement membranes seem to be most important for regenerating nerves.[17]

INDICATIONS

Assessment of the risk of extracapsular extension (ECE) prior to RP is essential, regardless of plans to perform nerve grafting.[25,26] At our institution, we currently employ a 12-core TRUS (transrectal ultrasonography)-guided biopsy template in which a medial and lateral core from each sextant are submitted for pathological review. Our pathologists report the number of positive cores and the length and percentage of tumor in each core. We combine this information, along with preoperative PSA and digital rectal examination (DRE) findings, in a nomogram that provides an estimate of the probability of ECE.[25,26] In addition, we often perform preoperative endorectal coil MRI of the prostate to evaluate for volume of cancer abutting the prostate capsule, which may indicate the presence of ECE, and for preoperative planning for dissection of the neurovascular bundle.[27] Based on these data, we counsel patients at high risk for ECE or tumor close to the neurovascular bundle that nerve resection may be necessary to obtain complete tumor extirpation and clear surgical margins. Such patients who are potent may be offered a nerve-grafting procedure in an effort to optimize potency, and, potentially, continence. Patients are then consented for unilateral or bilateral nerve grafting using either the sural or the genitofemoral nerves. If the caliber of the genitofemoral nerves is inadequate, the sural nerve may be harvested. The final decision to widely resect the neurovascular bundles may be made intraoperatively based on the adherence of the neurovascular bundles to the prostate and the palpation of the tumor within the prostate.

TECHNIQUE

The patient is placed supine on the operating table, and the right leg is prepped into the surgical field, even in cases of planned genitofemoral nerve harvesting, in the event the caliber of the genitofemoral nerves renders these inadequate for use as a donor nerve. Using the right leg allows sural nerve harvesting simultaneous to the prostatectomy once the decision has been made to resect one or both cavernous nerves. We conduct an extended pelvic lymphadenectomy, bilateral or unilateral wide-resection radical prostatectomy, and place the urethral anastomotic sutures prior to initiating the nerve-grafting procedure. Our radical prostatectomy technique has been described in detail elsewhere.[28] During the lymphadenectomy, the genitofemoral nerve is identified. In general, if the genitofemoral nerve is of sufficient caliber, it is considered adequate for nerve grafting; otherwise, the sural nerve should be used because its caliber is reliably large enough for the neural anastomosis. This final assessment is at the discretion of the surgeon. The advantage of use of a larger-caliber nerve is that if the distal cavernous nerve stump is indistinct, the larger-caliber donor nerve allows more leeway in achieving a successful graft-to-distal stump anastomosis. Prior to the apical dissection and pedicle dissections, the distal and proximal nerve stumps are identified using the CaverMap stimulator.[29,30] Prior to transection, the proximal nerve stump is marked with a 4-0 Prolene suture for identification later. The distal end may be marked with a 4-0 Prolene suture or small clip at the time of transection. The prostate is removed and the bladder neck is matured and the urethral anastomotic sutures are placed in the urethra and protected. Final hemostasis is secured. The nerve graft is then performed. If the nerve stumps cannot be adequately identified, the nerve graft procedure is omitted, as close apposition of nerve endings is essential for graft success. The gap is measured between the nerve stumps, and an appropriate length of nerve, approximately 20% longer than the gap, is then resected so as to perform a tension-free anastomosis. If the sural nerve is used, a curvilateral incision is made superior and posterior to the lateral malleolus and up to 30 cm of sural nerve is harvested.[7] When the sural nerve is harvested, the proximal and distal sural nerve stumps are thoroughly cauterized to prevent neuroma, then buried deeply within the gastrocnemius muscle. The grafts are fashioned to the appropriate length and anastomosed to the nerve stumps using 7-0 Prolene interrupted sutures through the epineurium with the orientation of the donor nerve reversed to avoid blind-ending nerve fascicles. At this point, 2.5–3.5× loupe magnifications are mandatory to optimally identify the nerve structures in the neurovascular bundle. Upon completion of the neural anastomosis, suction must be kept to a minimum to avoid disruption of the graft anastomosis; if suction is used, a trap is placed on the suction tubing. The bladder neck closure and vesicourethral anastomosis is then completed, drains are placed, and the abdomen is closed. In the event of unilateral nerve grafting, a single Jackson–Pratt drain is placed in the contralateral obturator fossa. In the event of bilateral nerve grafting, bilateral Penrose drains are placed. There are no special postoperative considerations except elevation of the foot the sural nerve is harvested from while the patient is recumbent. We encourage ambulation, starting postoperative day 1.

Laparoscopic and robot-assisted nerve graft procedures have been described and typically follow the tenets of the open procedure,[31–34] but the long-term efficacy is not yet established.

The role of nerve stimulation by the CaverMap nerve stimulator is controversial in terms of ultimate erectile outcome prediction, but it has been shown to have excellent sensitivity for identifying the neurovascular bundles. In a multi-institutional trial, Klotz et al[30] reported improved erectile function at 12 months as measured by RigiScan and Sexual Function Inventory Questionaire. Walsh and coworkers[35] found that the CaverMap device was able to identify the neurovascular bundle with a sensitivity and specificity of 88% and 54%, respectively. Kim and colleagues[36] reported a sensitivity of 77% for detection of the neurovascular bundle in their series of 60 radical prostatectomies. Rabbani et al have reported that the degree of response to intraoperative stimulation was associated with erectile function recovery.[37]

Based on cadavaric studies, Takenaka et al[38] have recently suggested that the pelvic splanchnic nerve fibers may join the neurovascular bundle as the cavernous nerve distal to the vesicoprostatic junction, the most usual place that the proximal stump is located and anastomosed during nerve grafting. These authors showed a ‘spray-like’ distribution of nerve fibers entering the neurovascular bundle at various points along its course. They suggested that nerve stimulation be conducted at the presacral and pararectal regions in addition to the proximal and distal neurovascular stumps to identify the areas of best stimulation so that the nerve graft will perform most effectively.

Graft-related complications are rare.[10,11,39,40] They include neuroma, mild paresthesia, along the nerve distribution, and sympathetic dystrophy in the ipsilateral lower limb.

RESULTS

Kim et al were first to describe bilateral sural nerve grafts for cavernous nerve interruption during RRP in humans.[13] In that early series, the authors reported that 1/9 patients had return of medically unassisted erections adequate for intercourse, and two additional patients had erections just below the normal threshold established by the International Index of Erectile Function (IIEF).[41] In an update of their series, Kim and collegues reported on 23 patients with a minimum of 12 months follow-up and found that 6/23 (26%) had medically unassisted erections.[42] An additional four patients were able to have intercourse using sildenafil, yielding a total of 43% with return of sexual function in their series, providing proof of concept. Functional return did not start until 5 months and plateaued by 18 months postoperatively. There were no graft-related complications, but both operative time and blood loss were higher in the grafted cohort.

Chang et al prospectively studied 30 patients with locally advanced prostate cancer who underwent RRP with bilateral wide excision of the nerve bundles and sural nerve grafting.[11] The authors used penile rehabilitation, starting 6 weeks postoperatively with RigiScan testing, to document erectile function. They found that 13/30 (43%) were eventually able to have intercourse, and 7/13 were able to do so without medical assistance.

More recent data do not appear to be as promising as earlier reports. Secin et al[43] reported that 34% of bilaterally nerve-grafted patients had recovered erections sufficient for penetration at 5 years, and only 11% of the cohort were able to consistently obtain erections adequate for intercourse. These inferior results may be due to less-stringent selection criteria, differing degrees of patient motivation, and potential differences between genitofemoral and sural nerve grafting success due to the difference in the caliber of the nerves.

While bilateral nerve grafting clearly may have some benefit, some have questioned the efficacy of unilateral nerve grafting. In a recent editorial, Scardino and Kim[39] argued that since approximately 30% of patients with unilateral nerve sparing were able to have medically unassisted intercourse compared with 55% of those who received unilateral nerve grafts, unilateral nerve grafting essentially has the same results as bilateral nerve-sparing surgery. At Memorial Sloan-Kettering between 1998 and 2002, 108 patients underwent unilateral nerve grafting after unilateral nerve resection and were compared with patients undergoing bilateral nerve sparing and with a historical cohort of patients undergoing unilateral nerve resection without grafting. At 4 years, 40% of unilateral graft patients had return of erections by IEFF erectile function (EF) domain score >17, compared to 80% with bilateral nerve sparing, and 25% with unilateral nerve sparing without grafting.[44] Canto et al[45] reported that 12/41 patients with unilateral sural nerve grafts regained potency compared with 3/34 with unilateral nerve sparing without grafting when erectile function was defined as ≥17 on the IEFF-EF domain score. Singh and coworkers[40] compared the urinary functional outcomes of 40 unilateral nerve graft patients to those of 40 unilateral nerve-sparing patients who did not undergo grafting. They defined continence as completely dry or occasional leakage of a few drops, and noted that 95% of patients with unilateral nerve grafting were continent at 12 months compared to 58% without grafts. Additionally, the authors found the UCLA Prostate Cancer Index (PCI) score was better; the median score was almost 10-fold higher for patients receiving unilateral nerve grafting compared to those who had unilateral nerve sparing with no nerve graft, even when age was entered into the model as a covariate.

Important limitations exist in human studies of cavernous nerve grafting. To date, most series have been modestly powered, single-institution experiences. No randomized trials have been reported to adequately answer the question of whether there is benefit to unilateral nerve grafting, although a randomized trail of unilateral nerve grafting is currently being conducted at MD Anderson Cancer Center. Selection of patients for unilateral nerve grafting may account for much of the reported potency recovery advantages. These patients tend to be young and sexually active preoperatively, and may be more motivated toward penile rehabilitation following RP.

CONCLUSIONS

Bilateral cavernosal nerve grafting appears to have some benefit in preservation of potency and, potentially, urinary continence in patients undergoing wide neurovascular resection at prostatectomy for locally advanced prostate cancer. The use of unilateral nerve grafting, while technically feasible, is controversial, but may potentially have an impact on erectile and urinary function recovery. More recent studies have shown inferior results compared to earlier pilot studies, possibly due to less-stringent patient selection as well as possible differences between sural and genitofemoral nerves being used as the donor nerve. Ultimately, randomized trials are necessary to determine the role of nerve grafting. In the future, the use of adjuncts such as neurotrophic growth factors may augment nerve grafts.

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CHAPTER 12

Management of intraoperative complications associated with open radical prostatectomy

Herbert Lepor

INTRODUCTION

An anatomical approach to radical perineal prostatectomy was described by Young in 1905.[1] Forty years later, Millin described the retropubic approach for radical prostatectomy.[2] The primary anatomical advantages of the perineal approach were avoidance of both a midline abdominal wall incision and the need to control the dorsal venous complex, which translated into less bleeding and a quicker recovery. Nevertheless, radical retropubic prostatectomy became the preferred approach by most urologists since they were generally more familiar with retropubic anatomy and the staging pelvic lymphadenectomy was readily performed through the lower midline incision.[3]

Historically, radical perineal and radical retropubic prostatectomies were associated with significant morbidity and mortality.[4] In the modern era, radical retropubic or perineal prostatectomy performed by expert surgeons is associated with exceedingly rare mortality and minimal morbidity.[5] The dramatically lower complication rates in contemporary series can be attributed to greater experience of individual surgeons, improved surgical technique, younger surgical candidates with less comorbidities, better anesthetic agents, and more sophisticated intraoperative monitoring.

In the period 1986–2006, the author personally performed over 3000 radical retropubic prostatectomies. Over 2500 of these cases were performed between 1994 and 2006 at the New York University Medical Center. The author has previously published a large retrospective and prospective outcomes assessment of 1000[6] and 500[7] cases, respectively. In both of these personal series, intraoperative and postoperative complication rates were exceedingly low. The low complication rates may be attributed to high surgical volume, thoughtful patient selection, rigorous preoperative assessment, meticulous surgical technique, and compulsive postoperative management. This chapter focuses on prevention and management of intraoperative complications associated with open radical retropubic prostatectomy, and draws on the extensive personal experiences of the author.

CARDIOVASCULAR COMPLICATIONS

Cardiovascular complications associated with radical prostatectomy include myocardial infarction, cerebrovascular accidents, cardiac arrhythmias, pulmonary embolus, and deep venous thrombosis. Since cardiovascular complications may occur intraoperatively and postoperatively, they will be discussed in this chapter.

In the modern era, these cardiovascular events are the primary cause of rare intraoperative and postoperative mortalities. For example, the author's only intraoperative or postoperative mortality in over 3000 cases occurred in an individual who experienced a myocardial infarction during his hospitalization and died at home within 30 days of surgery. The overall rates of deep vein thrombosis (0.1–2.3%), pulmonary embolus (0.0–2.0%), and cardiovascular complications (myocardial infarction and arrhythmias) (0.1–0.7%) reported by experienced surgeons is exceedingly low[6–10] (Table 12.1).

A detailed preoperative review of systems, social history, and family history should focus on identifying significant cardiovascular disease or associated risk factors. Risk factors include hyperlipidemia, hypertension, diabetes, smoking, and a family history of atherosclerotic vascular disease. The coexistence of erectile dysfunction may represent an early indicator of occult systemic vascular disease. Men with known cardiovascular disease or high-risk factors should undergo a thorough preoperative cardiovascular evaluation, including auscultation for carotid bruits, an echocardiogram to assess ejection fraction and cardiac wall motion, and an exercise stress test to identify cardiac ischemia.

Men with significant functional cardiac compromise or coronary artery disease generally should not be offered radical prostatectomy, since their limited life expectancy and increased surgical risks do not justify surgical attempts to cure the disease. Depending upon the aggressiveness of the disease, these men should be offered non-surgical options, including active surveillance, radiation therapy, or hormonal ablation. Men with evidence of coronary artery disease who are deemed appropriate candidates for radical prostatectomy should be carefully monitored intraoperatively to avoid sustained hypotension. A lower threshold should be established for transfusing blood products if bleeding occurs, in order to decrease myocardial ischemia. All men with pre-existing coronary artery disease should undergo serial electrocardiograms (ECGs) and cardiac enzyme monitoring immediately postoperatively, independent of their postoperative course. Identifying a myocardial infarction early in its course allows

Table 12.1 Cardiovascular complications following radical retropubic prostatectomy

Surgeon/institution	*DVT* (%)	*PE* (%)	*Cardiovascular*[a] (%)
Saint-Jean Cerou Languedoc[10]	2.3	0.8	0.2
Mayo Clinic[8]	1.3	0.7	0.7
Catalona[9]	–	2.0	0.1
Lepor[6]	0.1	0.1	0.7
Lepor[7]	0.4	0	0.4

DVT, deep venous thrombosis; PE, pulmonary embolus.
[a]Myocardial infarction and arrhythmia.

for immediate thrombolytic intervention, which may diminish mortality and damage to the myocardium associated with the event.

Any changes in mental status or extremity weakness should prompt immediate computed tomography (CT) of the head with contrast in order to identify a cerebrovascular accident. A thromboembolic event arising from a plaque in the carotid or basilar arteries or an intimal dissection of these vessels may represent the etiology for an intraoperative or postoperative cerebrovascular accident. A thrombus arising from the left atrium in association with atrial fibrillation is another relatively common cause of postoperative cerebrovascular accident. A hypertensive crisis or a right-sided embolus passing to the left side of the heart via a septal defect is a rare etiology for a cerebrovascular accident. An echocardiogram should always be obtained to exclude the heart as the source of the thrombus. In some cases, prompt initiation of anticoagulation may decrease the extent of the final neurological deficit.

Pulmonary embolus represents the most common life-threatening thromboembolic event associated with radical prostatectomy. In rare circumstances, the pulmonary embolus may occur intraoperatively. The role of prophylaxis for preventing pulmonary embolus and deep venous thrombosis is highly controversial.[11] The author personally does not recommend any routine pharmacological or mechanical prophylaxis for deep venous thrombosis or pulmonary embolus with the exception of compression stockings. A personal or family history of deep venous thrombosis should trigger a hematology consultation and a more aggressive preventive strategy, including mechanical compression boots and administration of low molecular weight heparin immediately after surgery if there is no evidence of postoperative bleeding. In our recent series of 500 consecutive cases of radical retropubic prostatectomy, only 0.4% of men experienced a deep venous thrombosis and none a pulmonary embolus within 30 days of the surgical procedure. We attribute our extraordinarily low rates of deep venous thrombosis and pulmonary embolus to avoidance of a staging pelvic lymph node dissection in almost 70% of men with Gleason score ≤6, a quick surgical procedure, early ambulation, short hospital stay, and encouragement for early return to activities.

INTRAOPERATIVE TECHNICAL COMPLICATIONS

Rectal injury

The rate of rectal injury during open radical prostatectomy in the modern era ranges between 0 and 0.6%[6–10] (Table 12.2). Rectal injury, if unrecognized intraoperatively, represents a very serious complication that may lead to sepsis and fistula formation.[12] In the setting where the

Table 12.2 Intraoperative technical complications during radical retropubic prostatectomy

Surgeon/institution	*Year*	*No. of patients*	*Rectal injury* (%)	*Ureteral injury* (%)
Saint-Jean Cerou Languedoc[10]	1992	620	0.5	0
Mayo Clinic[8]	1995	1000	0.6	0
Catalona[9]	1999	1870	0.05	0.05
Lepor[6]	2001	1000	0.5	0.10
Lepor[7]	2003	500	0	0.2

rectal injury is identified postoperatively and is associated with an abscess, a diverting colostomy is mandatory with incision and drainage of the associated abscess. The rectal fistula, if persistent, can be closed at a later time and the colostomy taken down. Some smaller fistulas will close spontaneously with prolonged urinary diversion.[13]

Historically, the standard of practice for all rectal injuries recognized intraoperatively was to primarily close the rectal injury and perform a diverting colostomy. Borland and Walsh[14] reported excellent outcomes with primary closure of the rectal injury and interposition of omentum between the rectal closure and the vesicourethral anastomosis. Excellent outcomes were achieved even in those men whose mechanical bowel preparation consisted only of Fleets enemas. It is often advisable to perform a colostomy if the rectal injury occurs in a previously radiated field.

In a recent personal series of 500 radical retropubic prostatectomies, the author identified only one intraoperative rectal injury, which was small and closed primarily in two layers without interposition of omentum. A pediculized flap of perirectal fat can be used in place of omentum, thereby obviating the need to open the peritoneum. In the above case, the adjacent perirectal soft tissue was simply imbricated over the rectal suture line. The wound was copiously irrigated and intravenous ampicillin and gentamicin was administered for 48 hours. The anal sphincter was manually dilated and the diet was limited to clear liquids for 48 hours. A meticulous effort was made to achieve a watertight vesicourethral anastomosis. Pelvic drains were removed per routine.

Rectal injury usually occurs while dissecting the apex of the prostate posteriorly. The injury is most likely to occur in men with small prostates, since the apex may not be easily discernible. Prior radiation therapy, underlying bowel disease such as ulcerative colitis or diverticulitis, and multiple prior transrectal biopsies are likely risk factors for rectal injury. In those high-risk cases for rectal injury, the dissection of the apex should be initiated laterally rather than in the midline.

Obturator nerve injury

The obturator nerve is most vulnerable during the pelvic lymphadenectomy. Injury to the obturator nerve is associated with the inability to adduct the thigh. Injury to the obturator nerve can be avoided if the nerve is always identified prior to ligating the nodal package inferiorly. The obturator nerve must be identified early in the course of the lymphadenectomy. The first step in the lymphadenectomy should be to bluntly sweep the lymph node package off the pelvic side wall and immediately identify the obturator nerve.

The author has no personal experience with injury to the obturator nerve. If identified intraoperatively, the nerve can be reappoximated using non-absorbable sutures. Obturator nerve injuries are often recognized postoperatively when the patient complains of the inability to adduct the lower extremity when attempting to transfer from the bed. In these cases, the injury often spontaneously resolves with limited functional deficit. Physical therapy may facilitate the return of lower extremity function.

Ureteral injury

Ureteral injury is a rare complication that occurs in 0–0.2% of cases[6–10] (see Table 12.2). Injury to the ureter may occur during an extended staging pelvic lymphadenectomy, during mobilization of the seminal vesicles, while dividing the prostatovesical junction, while obtaining hemostasis for brisk pelvic bleeding, or when performing the bladder neck reconstruction. Failure to observe a blue efflux from both ureteral orifices following administration of methylene blue or indigo carmine during the surgical procedure provides the opportunity to identify most ureteral injuries intraoperatively. If a blue efflux is not observed bilaterally, it is mandatory to pass a 5F feeding tube in order to confirm that the ureter is intact and not ligated. Depending upon the site and degree of injury, a ureteroneocystotomy, or ureteroureterotomy should be performed. In selected cases, deligation may be adequate. A ureteral ligation or transaction not detected intraoperatively typically presents with flank pain, a slight and transient increase in the serum creatinine, or persistent urinary drainage from the pelvic drains. Any one of these events should trigger a renal ultrasound in order to identify hydronephrosis and/or a contrast imaging study to identify urinary extravasation. A very slight and transient rise in serum creatinine may represent a unilateral ureteral ligation, whereas a marked rise in serum creatinine may represent a ureteral transection with intraperitoneal extravasation and reabsorption owing to an associated peritonotomy. A marked increase in serum creatinine most likely reflects prerenal azotemia or acute tubular necrosis.

The author has personally encountered only three ureteral injuries. One injury was identified intraoperatively and occurred while mobilizing the seminal vesicle. A ureteroneocystotomy with a psoas hitch reimplantation was performed without sequelae. The second injury occurred in an individual from Kenya who failed to divulge a history of schistosomiasis. The prostate and bladder were encased in extensive fibrosis and the ureter was ligated just outside the bladder. This individual postoperatively experienced flank pain and a slight elevation of the serum creatinine. A renal ultrasound revealed hydronephrosis. A ureteroneocystotomy was also performed without sequelae. A third patient presented 3 years following an uncomplicated radical prostatectomy. An abdominal CT scan was performed following a motor vehicle accident which revealed an atrophic kidney. Subsequent imaging studies demonstrated the site of ureteral obstruction to be just outside the bladder wall. The patient never experienced flank pain postoperatively despite what appears to have been a complete ligation of the ureter. Since the hydronephrotic kidney was atrophic and asymptomatic, no treatment was recommended.

Vascular injury

Injury to the external or internal iliac vesicles rarely occurs during radical prostatectomy. In cases where there is a laceration, the vessels should be repaired with appropriate vascular sutures. In rare cases when the external iliac artery or vein is inadvertently ligated, these structures must be repaired immediately to avoid ischemia to the lower extremity.

Hemorrhage

Historically, open radical retropubic prostatectomy was associated with significant bleeding. The description of the dorsal venous complex by Reiner and Walsh and a technique for its early control have greatly diminished the likelihood of encountering life-threatening intraoperative bleeding.[15] Significant intraoperative bleeding is more likely to occur in men with very large prostates,[16] in individuals with extensive perivesical and periprostatic venous tributaries, and in men with an unrecognized coagulopathy.

If the prostate exceeds 100 g, a row of hemostatic prostatic capsular sutures are placed on the anterior surface of the prostate in order to reduce back-bleeding prior to ligating the dorsal venous complex distally. In some cases, the prostate is so large it is not technically feasible to suture/ligate the dorsal venous complex prior to dividing this structure. In these cases, the dorsal venous complex is sharply divided and hemostasis is secondarily achieved. The urethra is then divided without pre-placement of the anastomotic sutures, and the apex is mobilized with care not to inadvertently enter the plane between the capsule and adenoma. The prostate is quickly mobilized off the rectum. With the Foley catheter retracted in a cephalad direction, the dorsal venous complex is controlled.

In cases where there are massive venous tributaries enveloping the bladder and prostate, attempts at achieving hemostasis with suture ligation may promote more bleeding. Efforts to achieve hemostasis may become futile and the surgeon must proceed expeditiously to complete the prostatectomy. Packing of the pelvis with lap pads during the prostatectomy will significantly reduce blood loss.

In rare cases, the surgeon may encounter diffuse small vessel bleeding that is refractory to attempts at hemostasis. If the bleeding cannot be controlled with suture ligatures, one should consider empirically transfusing platelets and clotting factors. The author recently experienced this scenario. An intraoperative coagulation profile was sent before the administration of platelets and clotting factors, which revealed disseminated intravascular coagulopathy.

Significant and potentially life-threatening hemorrhage may occur during the immediate postoperative period.[17] In most of these cases, meticulous hemostasis had been achieved prior to closing the abdominal wall incision. The signs of life-threatening postoperative hemorrhage include hypotension, tachycardia, and low urine output. In the majority of cases, these signs of life-threatening postoperative bleeding occur in the first 2–4 hours while the patient is in the recovery room. Central venous and arterial lines should be placed in order to facilitate monitoring of blood pressure and provide access for rapid volume replacement. If the hypotension, tachycardia, and low urine output do not respond rapidly to boluses of intravenous fluids, the surgeon should begin to make plans to return to the operating room even if multiple units of blood products have not yet been transfused. If there is a transient response to fluid expansion, the patient must remain in a monitored setting. Serial hematocrits should be obtained. In cases with significant bleeding, the response to intravascular fluid replacement is often transient. The volume of the pelvic drainage is a very unreliable indicator of significant bleeding. As the bleeding progresses, the abdomen becomes distended. The expanding hematoma exerts tension and may disrupt the anastomosis, which leads to greater abdominal distention as both urine and blood fill the pelvis. If the decision is made not to return immediately to the operating room, the patient should remain or be transferred to a monitored setting with repeat hematocrits obtained until stabilization is demonstrated and hypotension resolves. In the author's experience, only six (0.2%) men have returned to the operating room for control of life-threatening bleeding. This is similar to Walsh's reported reoperation rate of 1% for control of bleeding.[18] In our experience, the decision to return to the operating room was always made within the first 8 postoperative hours. Although it is difficult to provide absolute criteria for reoperation, this decision should be made before the patient has received extensive transfusions. As the amount of transfused blood products increases, the patient's clotting capacity further deteriorates. Whereas significant bleeding may eventually subside, the pelvic hematoma will probably cause a protracted clinical course due to anastomotic disruption, ileus, infection, and clot retention. Re-exploration with evacuation of the hematoma and repair of the anastomosis often expedites the recovery.[17]

Prior to re-exploration, large-bore intravenous access must be obtained with restoration of intravascular volume. It is also prudent to place an arterial line for blood pressure monitoring. Depending upon the volume of blood transfused, fresh frozen plasma, platelets, and calcium should be administered. In several cases requiring reoperation, we have identified an unrecognized coagulopathy such as factor 11 deficiency and Von Willebrand's disease.[17] In these cases, no active bleeding site was identified in the operative field. Replacement of clotting factors was the primary requirement for achieving hemostasis.

The incision is reopened and the blood clots evacuated. In many cases, the anastomosis is already disrupted due to the expanding hematoma. It is not possible to adequately explore the pelvis for bleeding with the anastomosis intact. Therefore, the anastomosis is always taken down and meticulous hemostasis secured. In the rare case where the bleeding is persistent and a specific site is not identified, the pelvis should be tightly packed and the incision closed with retention sutures. The author has resorted to this measure on only one occasion. The packing may be removed 24 hours later when the patient is hemodynamically stabilized. In our cases where the decision to re-explore was made relatively early, the patients were discharged within 48 hours after the reoperation and the catheter removed on the 7th postoperative day.

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CHAPTER 13

Radical perineal prostatectomy step by step

Paul McInerney

INTRODUCTION

The current philosophy of 'first do no harm' in the management of localized prostate cancer has resulted in a plethora of non-invasive or minimally invasive techniques which now rival radical prostatectomy. It has been suggested that in screen-detected, low-grade prostate cancer for individuals between 55 and 74 years of age, the disease-related death rate over a 15-year period is 1% and the benefit from radical intervention less than 1%.[1] We should therefore be offering the procedure only to specific at-risk groups and endeavor to achieve a complication rate of less than 1%.

Radical perineal prostatectomy was popularized by Hugh Hampton-Young[2] and throughout its history there have been notable modifications reported[3] and even a simple approach described for non-malignant disease.[4]

The appeal of the perineal approach has always been the belief that the procedure is less invasive than the retropubic approach and has a lower postoperative morbidity and, in the author's view, is equivalent to laparoscopic radical prostatectomy in many perioperative parameters.[5] Indeed a recent editorial comparing open, laparoscopic and robotic techniques affirmed: 'There is no doubt that as far as pain, complications, transfusion rate, continence, positive margins and cosmetics, radical perineal prostatectomy meets every goal of minimally invasive surgery'.[6]

SELECTION

Clinicians will vary in their selection criteria for radical prostatectomy, but there are certain specific criteria relevant to the perineal approach, which are as follows:

- Size matters. Prostates in excess of 80 cc are difficult to deliver through the male pelvic outlet and in the author's institution glands below 60 cc in size are approached perineally and above that size retropubically. Larger glands can be removed by the perineal route, but techniques such as bisection of the gland may need to be employed.
- Hip deformities. The extended lithotomy position is required to optimize access and individuals with limited hip flexion cannot be positioned satisfactorily.

- Previous transurethral resection of prostate. This is a relative contraindication and, certainly, when initially embarking on the procedure, the bladder neck fibrosis resulting from previous bladder neck surgery will make the procedure more difficult.
- Previous perineal sepsis. A more difficult dissection may be expected and more time should be allowed.
- Obesity. In the majority of cases perineal prostatectomy is still perfectly possible in the presence of obesity and is often a much safer approach to undertake in these circumstances than the retropubic.
- Prior laparoscopic mesh hernia repair. One in six men over 60 years old are likely to develop an inguinal hernia and, as the preperitoneal laparoscopic repair is increasing in popularity, the presence of a 13 × 11 cm mesh in the retropubic area makes retropubic prostatectomy all but impossible, but does not preclude the perineal approach.

PREOPERATIVE PREPARATION

- Bowel preparation – this is essential and will reduce the complication rate in the event of a rectal injury.
- Deep vein thrombosis prophylaxis – this is arguable in that the patient has two risk factors for thromboembolic disease – namely, cancer and pelvic surgery – but the prolonged lithotomy status does tend to keep the veins adequately drained down to the pelvic level.
- Anesthesia – general anesthesia is preferable, although in exceptional circumstances a spinal anesthetic with sedation can be appropriate.
- Epidural cannula – the use of an epidural cannula again is helpful in offering postoperative pain relief, but will potentially slow down patient ambulation in the postoperative period.

OPERATION

Step 1 – patient positioning

The extended lithotomy position is essential (Figure 13.1). The hips are hyperflexed with the knees almost impacting on the patient’s chest. A sandbag, or roll, is placed under the back to elevate the buttocks and the table angled in a Trendelenburg position of 10–20° to allow the perineum to be parallel to the floor. The patient is prepped and draped to allow exposure of the perineum and the genitalia. The Lowsley retractor (Figure 13.2) is placed urethrally in the same fashion as a urethral sound and the instrument is opened once the tip is in the bladder to allow control over the position of the prostate. (It is sometimes necessary to relax the position to allow easy passage of the instrument.) Some authors recommend prior cystoscopy to exclude urethral stricture or coincident bladder pathology.

Step 2 – incision (Figure 13.3)

The incision represents three sides of a rectangle based inferiorly on each side on the ischial tuberosity extending from a position horizontally in line with the anus and extending 4 cm above the anus. The wound is deepened through the ischiorectal fat and will include division of the so-called central tendon, which may be a well-represented structure in the midline or may be nebulous. Deepening the incision through the ischiorectal fat will allow the rectum to be untethered and displaced posterially to improve access.

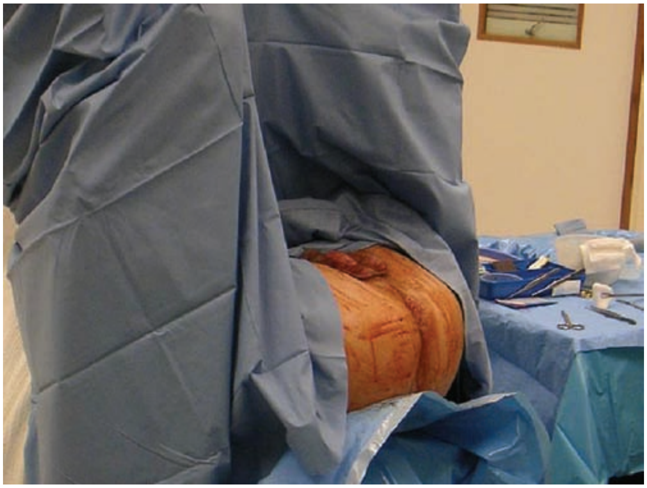

Figure 13.1 The extended lithotomy position enables the perineum to be aligned horizontally with the floor.

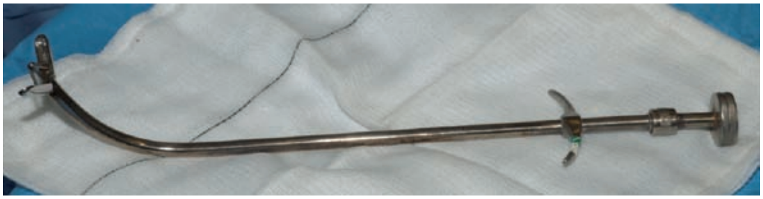

Figure 13.2 The Lowsley retractor is inserted prior to the incision or afterwards, as demonstrated.

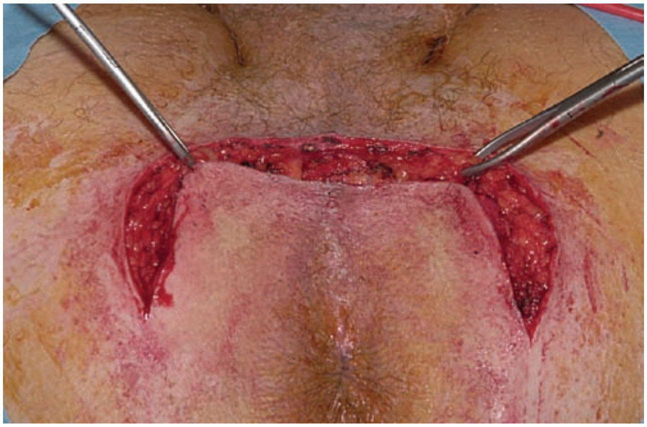

Figure 13.3 The incision starts above the ischial tuberosity on each side with its horizontal position 4 cm above the anal verge.

Step 3 – perineal body

The next landmark is exposure of the inferior portion of the bulbospongiosus muscle, which has a 'herring bone' appearance with the muscle fibers fanning superiorly either side of a white midline raphe (Figure 13.4). The most inferior point of this inserts into the true central tendon of the perineum, the perineal body. At this point two possible approaches are described. The trans-sphincteric approach involves access to the prostate from within the confines of the anal sphincter mechanism[3,7,8] the suprasphincteric approach, favored by the author, involves access from above the sphincter mechanism and therefore does not subject the patient to a risk of anal incontinence. This is the approach described.

Step 4 – the rectourethralis

Access to the perineum takes place in a plane between the midline raphe of the bulbospongiosus and the perineal body, below which lies the external sphincter mechanism. An incision is made with scissors along the fibrous tissue of the perineal body and gradually the urethra is dissected free from the anal sphincter mechanism by following the midline raphe, which extends horizontally in this position. On occasion, the tissue can be muscular and is effectively the rectourethralis muscle, but equally, this can be represented by a fine strand of spongy tissue, which is an extension of the spongiosus itself. Obviously, the use of the Lowsley retractor is helpful to prevent urethral injury during this part of the dissection and, equally, if there is a fear of rectal injury, a double-gloved finger in the rectum can demonstrate the position of this structure. This dissection allows quite a narrow channel to be forged to allow access to the layer of Denonvilliers' fascia overlying the inferior margin of the prostate and by manipulation of the Lowsley retractor, the rectum can be swept off the inferior margin of the prostate with blunt dissection. Great care has to be taken during this maneuver because rectal perforation is a possibility, albeit a rare one.

Step 5 – nerve preservation

Denonvilliers' fascia overlying the prostate is incised in the midline and the neurovascular

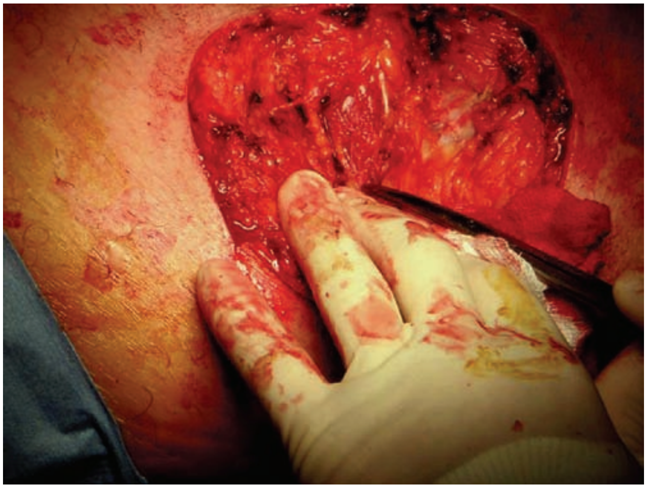

Figure 13.4 The perineal body is exposed. Trans-sphincteric or suprasphincteric approaches are possible.

bundles swept laterally if nerve preservation is intended. This allows exposure of the prostatourethral junction (Figure 13.5) and a right-angled retractor is advanced at the shoulder of the prostate around the urethra. The presence of the Lowsley retractor is a useful guide to confirm the posterior margin of the urethra and, once the urethra has been circumnavigated, a tape is placed around it to allow it to be retracted. Minimal dissection is undertaken at this point to avoid any damage to the sphincter.

Step 6 – urethral division

The urethra is incised at the prostatourethral junction, or in the case of larger prostates where extra urethral length is required, an additional few millimeters of urethra can be achieved by dissecting out the intraprostatic portion of the urethra, although the risk of urethral margin positivity is increased by this maneuver. Once the urethra has been transected and the Lowsley retractor removed, the prostate is pulled down into the wound, either by a 20F catheter with 20 ml in the balloon, or by use of a Young's bladder neck retractor.

Step 7 – dislocation from the pubis

Fibrous adhesions tether the anterior margin of the prostate to the back of the pubis and these can be freed by sharp dissection. At this point it is possible to breach the dorsal venous complex, but significant hemorrhage is a rare event and can usually be controlled by insertion of a swab. Lack of bleeding is in part due to the patient's position. Once these adhesions have been freed, the junction between the base of the prostate and the bladder becomes apparent and the 'valley' which represents the margin between the two structures can be developed all the way down to the bladder neck. Division of some of the lateral pedicle tissue on each side following diathermy can be useful in further mobilizing the prostate at this juncture. Liberal use of the diathermy does impair nerve preservation.

Step 8 – division of the bladder neck

Once the bladder neck is exposed, a right-angle retractor can be placed behind this, allowing the bladder neck to be divided and the catheter or Young's retractor is removed. The catheter

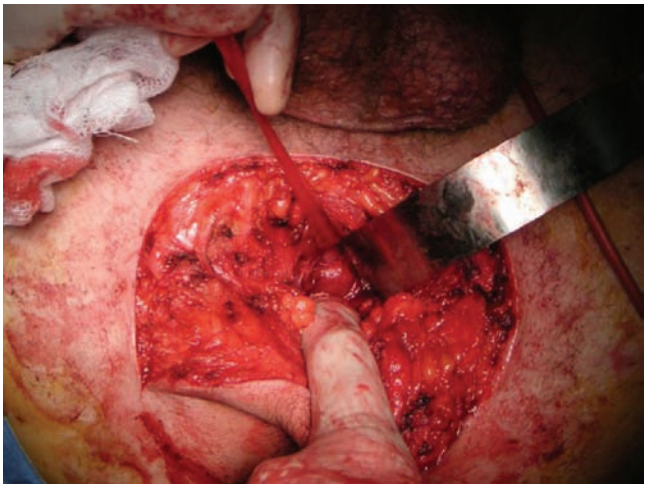

Figure 13.5 A tape is passed around the urethra and the prostatourethral junction exposed.

can be utilized as a retractor itself by flipping the tip out through the bladder neck and pulling it backwards over the anterior margin of the prostate to meet the drainage end of the catheter and a clip can then be used to retract the prostate away from the bladder. The plane between the trigone and the base of the prostate is then developed. The presence of significant middle lobe tissue can make this maneuver more difficult and it is possible to transect the middle lobe tissue and remove it subsequently once the prostate has been delivered. This is the part of the dissection that can be difficult in patients who have undergone previous transurethral resection of the prostate. Preservation of the bladder neck is an arguable benefit for subsequent continence and, again, a balance exists between positive margin status and bladder neck preservation.

Step 9 – division of vasa and delivery of seminal vesicles

Once the trigone has been pushed away from the base of the prostate by blunt dissection, the plane can be deepened to expose the ampulla of the vas and the base of the vesicles on each side; 1.5 cm of vas is exposed and divided between ligaclips. (Figure 13.6). Full exposure of the seminal vesicles requires further division of the lateral pedicles on each side and care must be taken because a significant artery is usually present lateral to the vesicles on each side and, once this is divided, the prostate can be advanced further. Complete excision of the vesicles is of arguable benefit, but it is certainly a satisfying maneuver to deliver the vesicles intact. If they are particularly tethered, then the vesicles are transected, again using ligaclips. Once the vasa, vesicles, and lateral pedicles have been divided on each side, the only remaining attachments of the prostate lie posteriorly and care must be taken to avoid damage to the rectum in dividing any remaining fascial strands. The radical prostatectomy specimen is then submitted for histology (Figure 13.7). Any bleeding encountered at this point is usually from the region of the tip of the vesicles and, once the prostate has been removed, access to this area is not difficult.

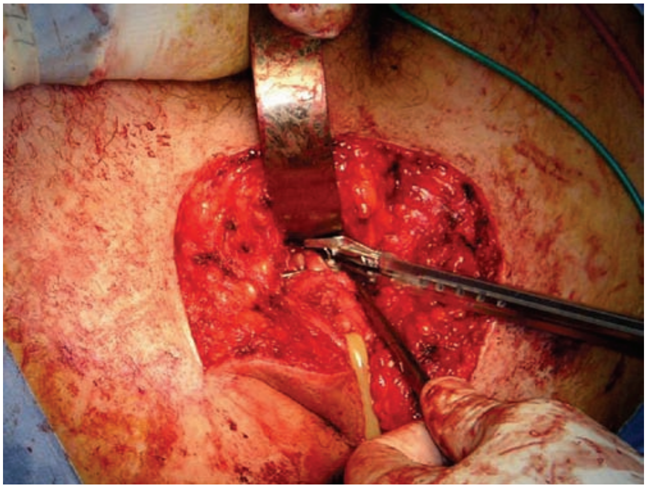

Figure 13.6 Once the bladder neck has been divided, the prostate is retracted posteriorly, the ampulla of the vas deferens and seminal vesicles are exposed on each side. Ligaclips are applied before transection of the vas.

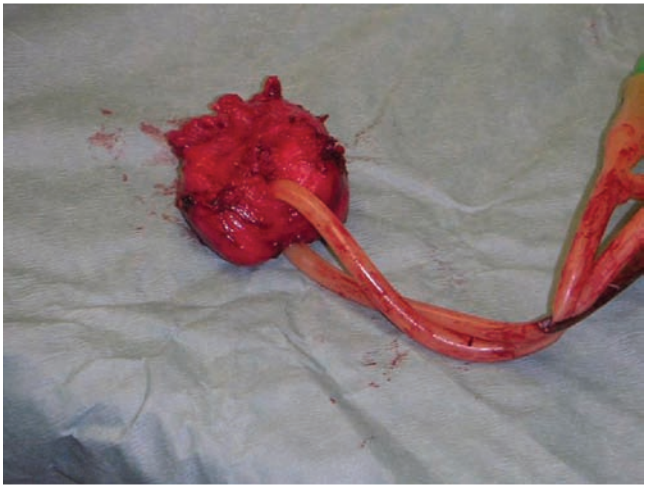

Figure 13.7 The radical prostatectomy specimen in this instance included the base of each seminal vesicle, but more complete excision is usually achievable.

Step 10 – bladder neck eversion

Some authors advocate sequential further excision of bladder neck tissue with frozen section analysis until margin negativity is achieved. If this is the case, then bladder neck reconstruction in a racquet-handle fashion may be required. If bladder neck preservation is intended, then the bladder mucosa at bladder neck level is everted by 4-6 fine (4.0) absorbable Vicryl (polyglactin) sutures, taking care not to compromise the ureteric openings. If full bladder neck preservation has been achieved, then visualization of the ureteric openings is not essential (Figure 13.8).

Step 11 – vesicourethral anastomosis

Anastomosis of the bladder neck to the urethra uses 6 × 3.0 Maxon (polyglyconate) or Monocryl (poliglecaptone) monofilament sutures. Prior eversion of the bladder neck makes this maneuver simpler. The first suture is placed at the 12 o'clock position and, unlike all the other sutures, it is actually easier to leave the knot on the inside. This suture is placed through the bladder neck initially and then clipped to the drapes to allow the insertion of the 10 o'clock and 2 o'clock sutures, which are also clipped to the drapes, and the Lowsley retractor or urethral sound is now reinserted to expose the cut end of the urethra. Retraction of the sphincter mechanism is helpful so that the sutures do not compress the sphincter and, ideally, the white fibrous urethra is all that is incorporated in the anastomosis. These three anterior sutures are all snugged down simultaneously and three further sutures are placed at the 8, 6, and 4 o'clock positions (Figure 13.9), taking care once again not to incorporate the ureteric openings. These sutures are not tied until the urethral catheter is inserted. An 18F catheter is inserted and if its position is satisfactory, the three sutures can then be tied down. The integrity of the anastomosis can then be checked by distending the bladder to check that a watertight closure has been achieved.

Step 12 – closure

A soft, rubber Penrose drain is placed behind the anastomosis and brought out through the corner of the wound (Figure 13.10).

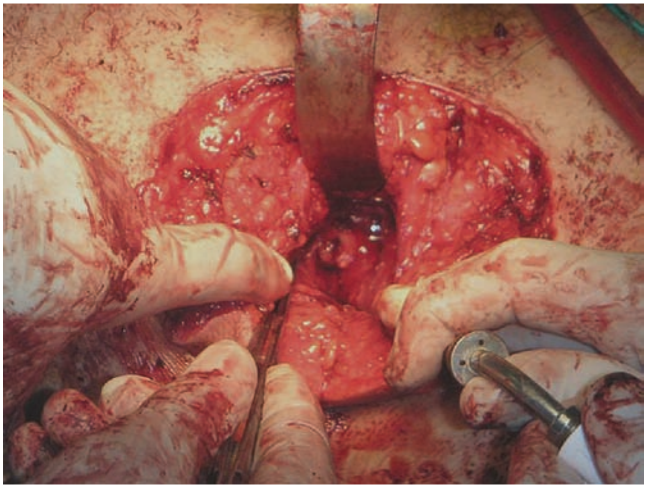

Figure 13.8 The everted bladder neck is easily identified prior to anastomosis to the urethra.

Reconstitution of the perineal body is by no means essential, but the ischiorectal fat is closed with interrupted Vicryl sutures. The skin is again closed by interrupted mattress sutures of a soft absorbable material, e.g. Vicryl rapide. It must be borne in mind that the patient has to sit on the wound and the use of clips or firm sutures can be uncomfortable.

POSTOPERATIVE CARE

The drain is not a closed system entity and has to be removed on the first postoperative day. The residual small defect does allow dependent drainage of any residual hematoma.

Early ambulation is encouraged. Patients are warned that the first bowel action is ‘a bit of

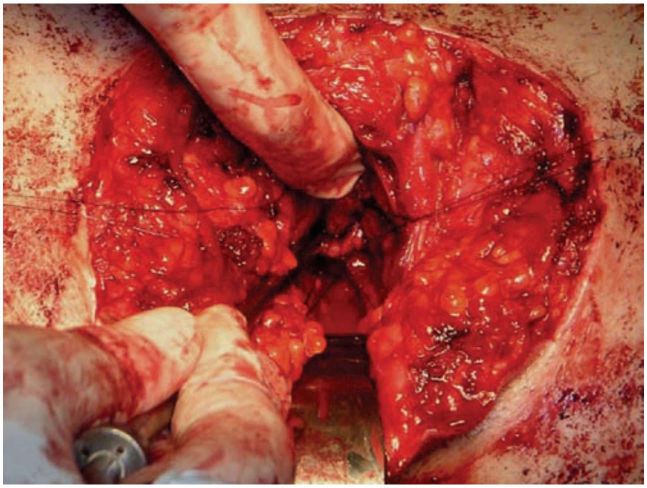

Figure 13.9 Good mucosal apposition is achieved because the urethra and bladder neck are easily approximated. The inferior sutures are tied after insertion of the urethral catheter.

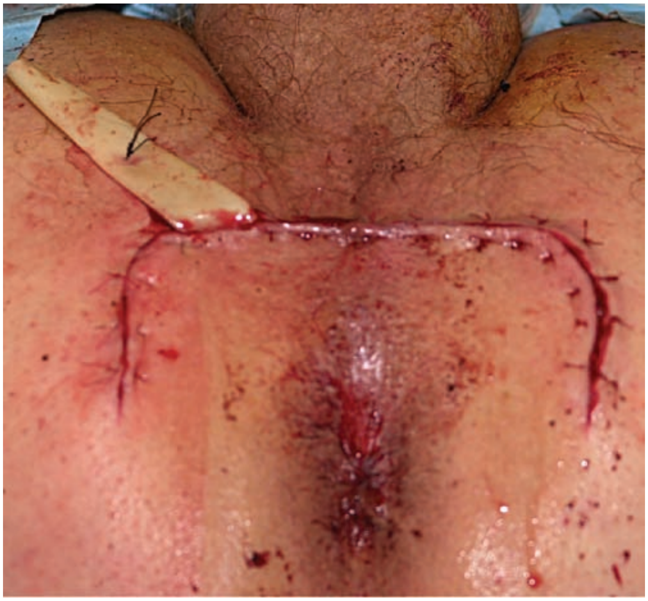

Figure 13.10 The wound is closed. A small defect is left for emergence of the Penrose drain.

an event'. Analgesia is given as required, but per rectal suppositories are to be avoided. The optimum timing of catheter removal is debatable. The author tends to leave the catheter in for 4 weeks so that the fear that most patients have of incontinence is not realized as the aftermath of the neurapraxia, which occurs as a result of the retraction, and has usually completely resolved by this stage. However, early catheter removal is feasible at the patient's request, but the patient should then be warned that immediate continence is less likely. Blood transfusion is rarely necessary, as average blood loss is usually between 200 and 400 ml.[9]

COMPLICATIONS

- Wound infection – in the author's series, a wound infection rate of 4% has been encountered. Simple wound toilet is usually all that is necessary because of the dependent drainage afforded by the position of the incision.
- Anastomotic leak – 3.4% of patients have a transient leak in the early postoperative period and this can be managed by bed rest.
- Sciatica – 1% of individuals will encounter this because of the exaggerated lithotomy position. Operative time will have a bearing on the risk, but so far no cases of compartment syndrome have been encountered.
- Incontinence – 4% of patients report incontinence lasting longer than 12 months.
- The level of incontinence varies between perineal prostatectomy series and an incidence between 3% and 25% at one year appears to be the reported range.[10,11] It should be borne in mind that there can be variation between patient-reported and surgeon-reported incontinence.[12]
- Impotence – the author has not been able to match the very encouraging potency results from some retropubic nerve-sparing series,[13] but age and nerve preservation are clearly important factors predicting the

return of potency. It remains to be seen whether prophylactic PDE$_5$ (phosphodiesterase E$_5$) inhibitor usage is helpful in the early recovery of sexual function.

- The size of the gland affects the outcome. Smaller glands are associated with better never preservation. Return of potency following radical perineal prostatectomy is not a rapid process and may take up to 18 months.[11] Bilateral nerve sparing, where possible, is superior to unilateral nerve sparing, in keeping with the results from retropubic surgery.[14]
- Orgasm – the loss of the seminal vesicles means ejaculation is absent, but the sympathetically mediated orgasmic function is often better preserved than the parasympathetically mediated erectile function.

OUTCOMES

There is no doubt that when it comes to outcomes, experience counts.[15,16] Most series show a decrease in positive surgical margins with time, but stage migration and improved patient selection may contribute rather more than surgical technique.[16,17]

Margin positivity rates are influenced by tumor stage but reportedly range from 6 to 64% for all pathological stages but 6.9 to 18.6% specifically for pT2 disease.[10,18]

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Part 4: Laparoscopic radical prostatectomy

CHAPTER 14

Laparoscopic radical prostatectomy step by step: Transperitoneal approach

Karim Touijer and Bertrand Guillonneau

INTRODUCTION

Better understanding of the intricate pelvic and periprostatic anatomy, with continuous refinements of the surgical technique and the integration of the laparoscopic approach, have significantly impacted the surgical treatment of prostate cancer. Consequently, the operation is performed today with better cancer control,[1,2] lower morbidity,[2] and improved quality of life outcome.[3,4] Since the description of the 'Montsouris technique' 8 years ago,[5] laparoscopic radical prostatectomy has been widely and regularly performed and has known a number of technical variations: transperitoneal or extraperitoneal, antegrade or retrograde, pure laparoscopic or robotic assisted….

Herein we describe step by step the transperitoneal antegrade laparoscopic radical prostatectomy technique as currently performed at Memorial Sloan-Kettering Cancer Center and debate the pros and cons of our present approach.

PREOPERATIVE

Indication

Patients with clinically localized prostate cancer and a life expectancy greater than 10 years are potential candidates for a laparoscopic radical prostatectomy. There are no 'technique-specific' contraindications to the transperitoneal laparoscopic approach. However, extensive prior pelvic surgery, prior prostate surgery, pelvic radiation therapy, or morbid obesity can raise the difficulty level of the procedure.

Patient preparation

Preoperatively, patients receive an enema. Thromboprophylaxis is ensured with sequential compressive devices placed on both calves and low molecular weight heparin administered prior to surgery then daily afterwards until discharge from the hospital. A single preoperative dose of an intravenous second-generation cephalosporin is given prior to skin incision for antibiotic prophylaxis.

SURGICAL TECHNIQUE

Positioning (Figure 14.1)

Under general anesthesia, the patient is positioned in a low lithotomy position with both arms set along the body. All the pressure points are adequately padded, and the patient is secured to the operating table with surgical

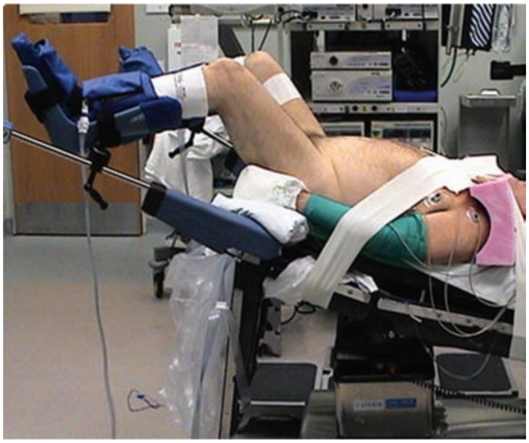

Figure 14.1 Patient positioning.

tape. One monitor is placed between the patient's legs, at the surgeon's eye level, and as close as necessary.

Trocars placement (Figure 14.2)

After a periumbilical incision, the pneumoperitoneum is insufflated through a Veress needle and set at a pressure of 12 mmHg. We use five trocars, one 10 mm and four 5 mm. The 10 mm trocar is inserted at the umbilical incision for passage of the 0 degree laparoscope, a thorough exploration of the peritoneal cavity is performed, and the patient is placed in the Trendelenburg position. The 5-mm working ports are then inserted under direct vision: in the left iliac fossa, the right iliac fossa, at McBurney's point, and halfway between the umbilicus and the pubic symphysis. The surgeon uses the scissors and bipolar cautery forceps; the assistant uses the laparoscopic suction device and graspers.

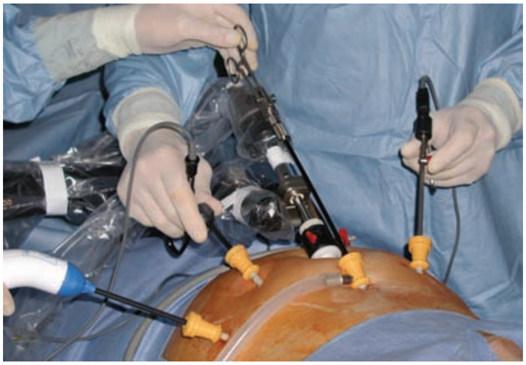

Figure 14.2 Trocars placement.

First step: pelvic lymph node dissection (Figure 14.3)

A standard bilateral pelvic lymph node dissection is performed on all patients, and includes the external iliac, the hypogastric, and obturator fossa nodal groups. The peritoneum lateral to the medial umbilical ligament is opened and all the lymphatic and fatty tissue lateral to the medial umbilical ligament, medial to the lateral pelvic side wall, distal to the iliac vessels bifurcation, proximal to Cooper's ligament, inferior to the external iliac vein, and superior to the hypogastric artery is removed. In high-risk patients, the nodal tissue over the common and external iliac arteries is removed as well. Large lymphatic vessels are clipped with 5-mm Hemolock while the small vessels are sealed with bipolar coagulation.

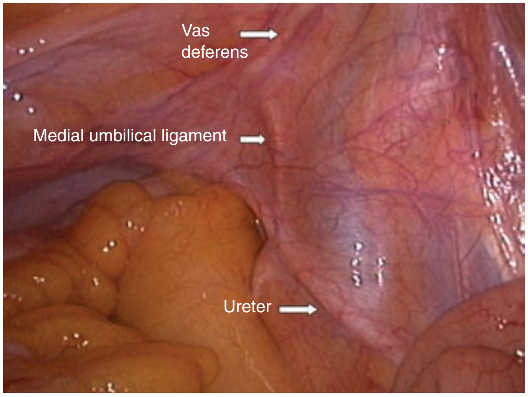

Figure 14.3 Landmarks for a pelvic lymph node dissection.

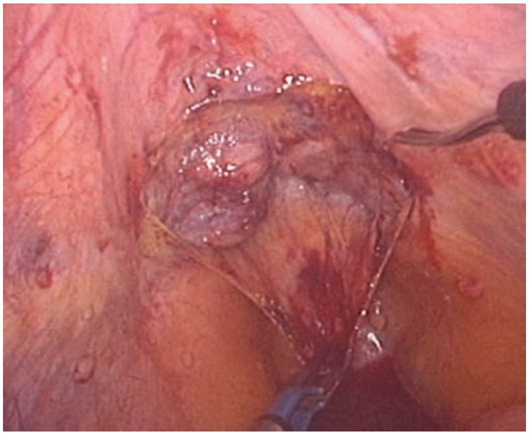

Figure 14.4 Posterior approach to the seminal vesicles.

Second step: posterior approach to the seminal vesicles (Figures 14.4 and 14.5)

Incising the cul-de-sac of Douglas

The assistant retracts the bladder anteriorly and the sigmoid colon cephalad. Often, for an adequate exposure, it is necessary to sharply dissect the sigmoid-parietal adhesions when present. The surgeon incises the posterior vesical peritoneum transversally approximately 1–2 cm above the cul-de-sac of Douglas. This exposes Denonvilliers' fascia covering the vasa deferentia and seminal vesicles. This step could be omitted if the patient's body habitus does not allow an easy access to the cul-de-sac of Douglas or when nerve-sparing surgery is not considered.

Freeing the seminal vesicles

Once the peritoneum is opened, the outlines of the seminal vesicles and vasa deferentia are clearly visible through Denonvilliers' fascia. The vasa deferentia are dissected and coagulated with bipolar forceps, then transected. One must be aware to carefully coagulate the deferential artery running along on the opposite side. Division of the vasa deferentia allows access to the seminal vesicles: the latter should be dissected along their surface to individualize their arterial supply, since it is important that these arteries are meticulously coagulated with the bipolar forceps facing the seminal

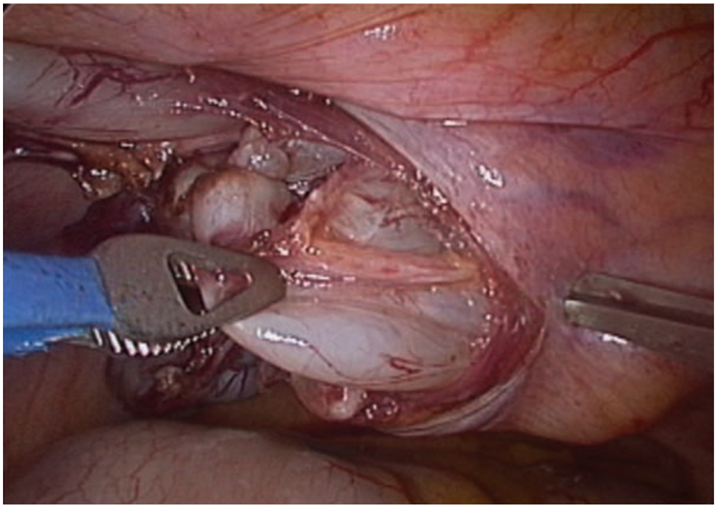

Figure 14.5 Dissection of the seminal vesicle artery.

vesicles to avoid any thermal injury to the inferior hypogastric plexus in close proximity. The use of surgical clips is a reasonable option for the control of the largest vesicular vessels. The seminal vesicles are then completely mobilized, with the prostate as their sole attachment.

Third step: anterior approach to the prostate (Figure 14.6)

Entering Retzius' space

The anterior parietal peritoneum is incised lateral to each umbilical ligament, and a plane of cleavage between the bladder and the anterior abdominal wall is reached and allows access to the preperitoneal space. The medial umbilical ligaments and the urachus remain intact (urachal sparing technique).

Exposing the endopelvic fascia

The fat over the fascia covering the prostate must be swept up laterally in order to expose clearly the intrapelvic fascia and the puboprostatic ligaments. The superficial dorsal vein is easily identified and coagulated with bipolar forceps. The endopelvic fascia is identified lateral to the prostate, and incised on its line of reflection, uncovering the levator ani muscle fibers. The medial attachments of the puboprostatic ligaments are not incised and the dorsal vascular complex is not ligated at this time or divided. All attempts are made not to dissect the apical sphincteric complex.

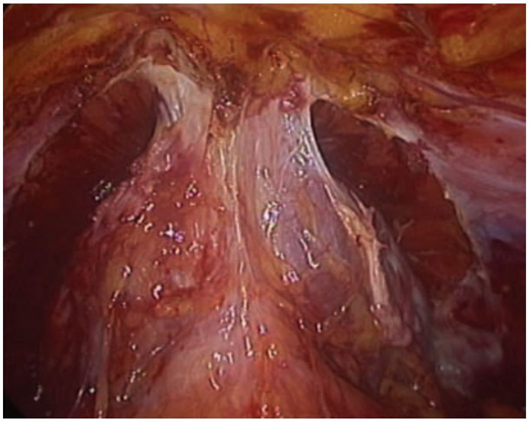

Figure 14.6 Incison of the endopelvic fascia.

Fourth step: bladder neck dissection

The anatomical landmarks of the bladder neck are easily identified once the anterior preprostatic fat is retracted cephalad, creating a faint outline of the anterior vesicoprostatic junction. The place where the bladder neck should be dissected is exactly where the fat becomes adherent to the detrusor muscle. The bladder neck is incised transversally and the tip of the catheter is pulled up by a grasper via the suprapubic port, to lift up the prostate and expose the posterior aspect of the bladder neck, allowing the surgeon to incise the posterior bladder neck and separate the bladder from the prostate. Posterior to the posterior bladder muscular wall, one reaches an important landmark to access to the seminal vesicles complex. Longitudinal muscular fibers between the prostate base and the bladder neck and this layer, easily recognizable, should be incised in order to gain access to the (previously dissected) retrovesical space. The vasa deferentia and the seminal vesicles are then simply brought into the operating field. This maneuver exposes on both sides the lateral prostatic pedicles. For oncological principles, we must clearly state that no effort is made to spare the bladder neck.

Opening Denonvilliers' fascia

The assistant pulls the vasa deferentia upward and places Denonvilliers' fascia on tension. The fascia is then incised sharply, bringing into view the prerectal fatty tissue. The incision is extended laterally and following the prerectal fat, the rectum is bluntly separated from the

Denonvilliers' fascia and the posterior surface of the prostate anteriorly.

Fifth step: lateral dissection of the prostate (Figure 14.7)

Preserving the neurovascular bundles: interfascial technique

The assistant grasps the vas and the seminal vesicle and pulls them medially. The inferior and medial landmark is easily identified by the posterior layer of Denonvilliers' fascia, the superior and medial landmark is delineated by incising the periprostatic fascia along the prostate from the base to the apex. The lateral prostatic pedicle is controlled high on the base of the prostate, theoretically at a safe distance from the neurovascular elements of the bundle. Because of the traction on the seminal vesicles, the prostatic pedicle appears to rise vertically, which facilitates their exposure but distorts their normal anatomical orientation. It is therefore important for the surgeon to reorient himself constantly during the dissection of the pedicles and be cognizant of the exact location of the neurovascular bundle.

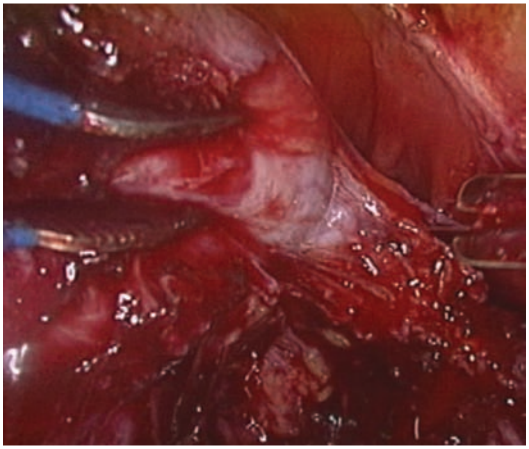

Figure 14.7 Dissection of the right neurovascular bundle.

Once the pedicle is controlled (with bipolar coagulation or clips, according to the surgeon's preference), the two fascial incisions – superior (periprostatic) and inferior (Denonvilliers' fascia) – can be joined to develop, with blunt dissection, the avascular interfascial plane, leaving lateral and posterior the neurovascular bundle recovered by a fascia, which reduces as much as possible the risk of mechanical injury to the bundle.

It is preferable to continue the apical dissection of the bundle after transecting the dorsal venous plexus, which gives mobility to the gland and facilitates the exposure of the apical and the distal third of the prostate.

Non-nerve-sparing procedure

If nerve sparing is not considered, the procedure differs: the prostatic pedicles are transected further lateral from the prostate and the posterolateral attachments of the prostate are not dissected but simply controlled (using bipolar coagulation or clips) and divided. It is important to remember that, if this step looks easier, the risk of rectal injury is higher because the dissection is performed close to it, in the perirectal fat.[6]

Sixth step: apical dissection of the prostate (Figure 14.8)

At this time, the only remaining prostatic attachments are the dorsal vascular complex, the urethra and the rectourethralis muscle, and the distal portion of the neurovascular bundles.

Division of the dorsal venous complex

The pneumoperitoneal pressure is temporarily increased up to 20 mmHg during this step, and the puboprostatic ligaments and the dorsal vascular complex are sharply divided perpendicularly to the urethra. This dissection is taken

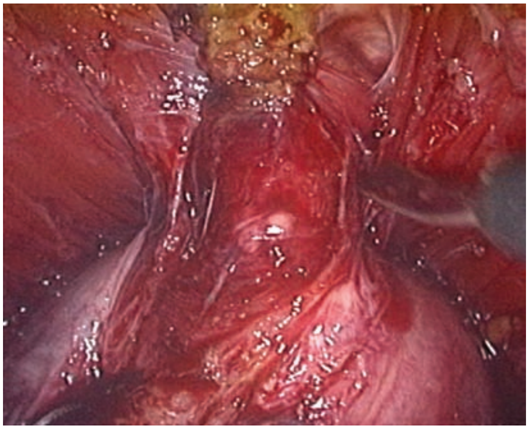

Figure 14.8 Apical dissection.

directly into the lumen of the venous plexus and, often, one or two arteries are encountered, necessitating selective use of bipolar cautery. The incision is tangential to the prostate to avoid iatrogenic incision into the prostatic tissue at the apex anteriorly, and to preserve the functionality of the membranous urethra distally. A Béniqué sound placed in the urethra helps to expose the anterior and lateral urethral walls.

The lumen of the veins of the dorsal vascular complex are then electively ligated with a 3-0 Vicryl (polyglactin) on an RB1 needle.

Division of Denonvilliers' fascia at the apex

At the apex, the neurovascular bundles are divergent from the prostate, but must be followed until their entrance into the pelvic floor, below and lateral to the urethra; the key element in this dissection is to follow the anatomical contours of the prostate. This dissection allows a safe exposure of the posterior urethra, and the remainder of Denonvilliers' fascia and the rectourethralis muscle fibers are divided.

Incising the urethra

The prostate is pulled cephalad and the urethra is then sharply incised with laparoscopic scissors under direct vision, following the shape of the prostate, particularly posteriorly where the apex could extend more distally.

The specimen is then placed in a laparoscopic bag, using a 5-mm scope inserted through a lateral port and the whole is extracted through an extension of the 10-mm periumbilical incision. The periumbilical incision is closed with two running sutures of 0 Vicryl, around the 10-mm trocar, and the pneumoperitoneum is reinsufflated.

Seventh step: specimen macroscopic examination (Figure 14.9)

The specimen is retrieved prior to starting the anastomosis. A macroscopic examination of the gland is performed, looking for any suspicious areas of positive surgical margins; confirmatory frozen sections are obtained when necessary.

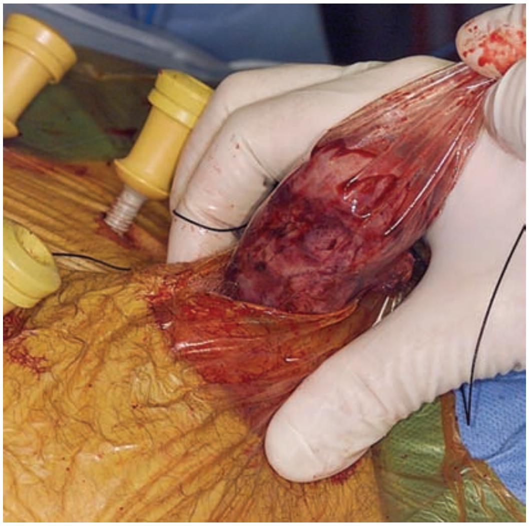

Figure 14.9 Specimen extraction through the periumbilical incision.

Eighth step: urethrovesical anastomosis (Figure 14.10)

The bladder mucosa is never everted. In cases with a large bladder neck, an anterior tennis racket reconstruction is required. For the anastomosis, the surgeon works with two needle-holders, using a 3-0 resorbable suture on an RB1 needle and all the sutures are tied intracorporeally. The Béniqué sound is used to help guiding the needle into the urethra in the correct location. The first four sutures are posterior, placed between the 5 and 7 o'clock positions, going inside-out on the urethra and outside-in on the bladder neck. These posterior surgical knots are therefore tied intraluminally. Four other sutures are symmetrically placed at the 4 and 8, then the 2 and 10 o'clock positions, and tied outside the lumen, starting outside-in on the bladder and inside-out on the urethra.

Three final anterior stitches are placed at the 11, 12, and 1 o'clock positions, going outside-in on the bladder and inside-out on the urethra. These three anterior sutures are anchored to the fascial edges of the dorsal vascular complex, then tied to place the bladder junction in a more anatomical and fixed position. The Foley catheter is inserted, the bladder filled with 180 cc of saline to confirm the correct position of the catheter, ascertain a watertight anastomosis, and wash out clots. At last, the balloon is inflated with 10 cc.

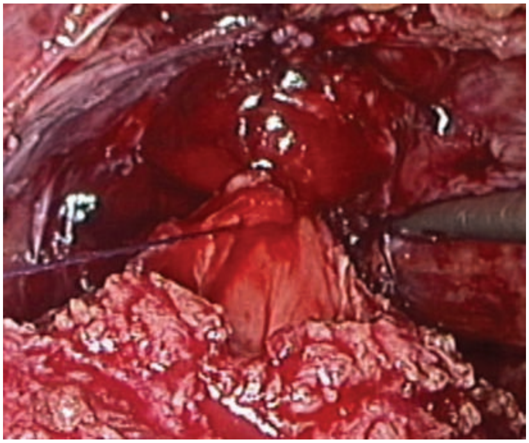

Figure 14.10 Urethrovesical anastomosis.

Completion of the operation

One or two suction drains are placed, one anterior in Retzius' space, and one posterior through the incision of the cul-de-sac of Douglas. The abdominal pressure is then lowered to 5 mmHg to check for venous bleeding and the 5-mm trocars are removed under direct vision and the port sites are once more checked to exclude vascular injury, particularly of the epigastric vessels. At the end, the incisions are conventionally closed and dressed.

DISCUSSION

In our hands the technique of transperitoneal laparoscopic radical prostatectomy has always been a continuous evolutionary process aimed at improving surgical quality and subsequently the postoperative results. The optimal outcome of radical prostatectomy is a total excision of cancer with the least morbidity and full recovery of continence and potency altogether and not individually.[7]

Efforts of continuous quality improvement, including review of the intraoperative video documentation, and critical multidisciplinary meeting between surgeons, pathologists, and radiologists all dedicated to the diagnosis and treatment of prostate cancer, has led to a significant decrease of the positive surgical margin rate over time, overall, and in pathologically organ-confined disease.[8,9]

In pursuing with the same thought, our preference for the transperitoneal approach is justified by our belief that a thorough pelvic lymph node dissection, including the external iliac, obturator, and hypogastric nodal group, cannot be completed extensively by laparoscopy through the extraperitoneal approach. Such a template is the original template and has constituted for years the standard pelvic lymphadenectomy for prostate cancer.[10–12] As demonstrated by others, any pelvic lymph node dissection short of the above-mentioned nodal groups is inadequate.[13–15] Certainly, the presence of lymph node metastases is a negative prognostic factor and lymphadenectomy remains largely a staging procedure; however, in men with nodal micrometastases only, the therapeutic benefit could not be ignored.[13,14,16] In our experience, a lymph node dissection that includes the external iliac, obturator, and hypogastric lymph node groups yielded positive nodes more frequently and retrieved a higher total nodal count than the often-performed pelvic lymph node dissection limited to the external iliac nodes.[17]

On the other hand, published studies comparing the transperitoneal vs the extraperitoneal laparoscopic approach failed to show any significant difference between the two approaches and the debate was deemed a 'false debate'. There is no doubt that symptoms from a urethrovesical anastomotic leak or postoperative bleeding are more pronounced and associated with more secondary complications after a transperitoneal approach than after an extraperitoneal one, but this statement cannot be a waiver for any oncological compromise. The issue of the quality of the pelvic lymph node dissection was not addressed by any of the studies.[18,19]

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CHAPTER 15

Laparoscopic radical retropubic prostatectomy step by step: Extraperitoneal technique

Jens-Uwe Stolzenburg, Evangelos N Liatsikos, and Chris Anderson

INTRODUCTION

Laparoscopic radical prostatectomy (LRP) and endoscopic extraperitoneal radical prostatectomy (EERPE), both considered to be among the most technically demanding laparoscopic procedures in urology, have been established as standard procedures routinely performed as first-line therapy for the treatment of localized prostate cancer at specialized centers.[1–4] The major advantages associated with minimally invasive laparoscopy are – among others – lower intraoperative bleeding rates, less postoperative pain, a shorter period of urethral catheterization, and a shorter hospital stay. The transperitoneal approach to an extraperitoneal organ may cause intraperitoneal complications such as bowel injuries, peritonitis, postoperative ileus, peritoneal adhesions, intraperitoneal bleeding, or intraperitoneal urine leakage.[5,6] We thus advocate the use of the extraperitoneal route for the performance of the laparoscopic procedure.[7]

Raboy et al described the first case report of extraperitoneal laparoscopic radical prostatectomy,[8] and Bollens et al described the first series of cases using this technique.[9] In 2002, we initially reported our technique and experience with the EERPE.[10] In 2003, we described our initial experience with 70 EERPE by an entirely extraperitoneal retropubic approach for radical prostatectomy.[11]

Since then we have continuously improved the technique, and it has been standardized as a first-line therapy for localized prostate cancer.[12] With increasing experience in performing EERPE, we were able to develop a nerve-sparing approach (nsEERPE) that we applied routinely in selected patients.[13] In addition, a puboprostatic ligament spearing technique has been developed that possibly enhances recuperation of early continence after surgery, without hindering the final oncological outcome of the procedure.[14]

The indications for EERPE are the same as for open radical retropubic prostatectomy. Clinically localized prostate cancer (T1 and T2) and a life expectancy of at least 10 years are two most important indications for treatment. From a technical point of view, EERPE can also be performed for clinical T3 cancer but requires increased surgical experience and should be avoided by beginners. The same applies to salvage prostatectomy after brachytherapy, external beam radiotherapy, or after high-intensity focused ultrasound (HIFU).

There are no specific selection criteria or special contraindications for EERPE. Previous abdominal surgical procedures do not affect the overall operative times or the complication rates.[15] Mesh placement from previous totally extraperitoneal hernioplasty (TEP) or transabdominal preperitoneal hernioplasty (TAPP) has been considered a contraindication for laparoscopic radical prostatectomy.[16] Nevertheless, although certain problems are presented by previous TEP/TAPP, it is feasible to perform EERPE. By adapting port placement and surgical technique, the operation can be performed safely and with good operative outcome.[17]

Despite the different techniques for radical prostatectomy, the key for better results is the understanding of the anatomy of the bladder neck and the urethra. Various studies have examined closely the anatomy of the neurovascular bundle (NVB) and the cavernosal nerves, but there is still no unanimous acceptance of nomenclature pertaining to the prostate's adjacent fascias and of the level of dissection for a nerve-sparing procedure. According to Walsh,[18] the NVB is located posterolaterally and symmetrically to the prostate between the two layers of the lateral pelvic fascia: levator fascia, lateral layer; prostatic fascia, medial layer.

Menon et al described their experience with the robotic technique and advocate that the neurovascular bundles are enclosed within the layers of the periprostatic fascia.[19] The layers of the periprostatic fascia merge with the anterior layers of Denonvilliers' fascia lateral to the prostate, forming a triangular space. The three sides of the triangular space are formed by the inner layer of the periprostatic fascia (prostatic fascia – medial vertical wall), the outer layer of the periprostatic fascia (levator fascia – lateral wall), and the anterior layer of Denonvilliers' fascia (posterior wall).

Kiyoshima et al proposed the wide dissection of the lateral aspect of the prostate during radical prostatectomy to ascertain NVB preservation. Although the NVB was thought to exist locally near the posterolateral region, it was found on the posterolateral region of the prostate in only 48% of the cases. In the remaining 52%, the nerves were spread on the entire lateral aspect of the prostate without either specific localization or bundle formation.[20]

It has not been clearly proven if these lateral nerves are responsible for continence or erectile function. Nevertheless, the presence of nerves is clear and there is a tendency to maintain as many nerves possible during a nerve-sparing procedure. For this reason, we always perform an intrafascial nerve-sparing technique[21] during nerve-sparing prostatectomy, leaving intact puboprostatic ligaments, the endopelvic fascia, the periprostatic fascia, and the neurovascular bundles, as described in the following paragraphs. Today, our experience is based on a series of 1500 patients who underwent minimally invasive radical prostatectomy using this entirely extraperitoneal retropubic approach.

TECHNIQUE – STEP BY STEP

Patient positioning

EERPE is usually performed with the patient under general anesthesia. Patients are placed in a dorsal supine position with legs slightly apart, as shown in Figure 15.1. The laparoscopic tower is placed at the bottom of the operating table and the patient in a supine position with a 10° head-down tilt. Both arms must be well protected, positioned on the body of the patient. The surgeon stands to the left of the patient with the assistant opposite. The camera-holder stands behind the head of the patient. The patient is draped to the operating table with a chest belt. In addition, both legs are draped on the table as well, minimizing the possibility

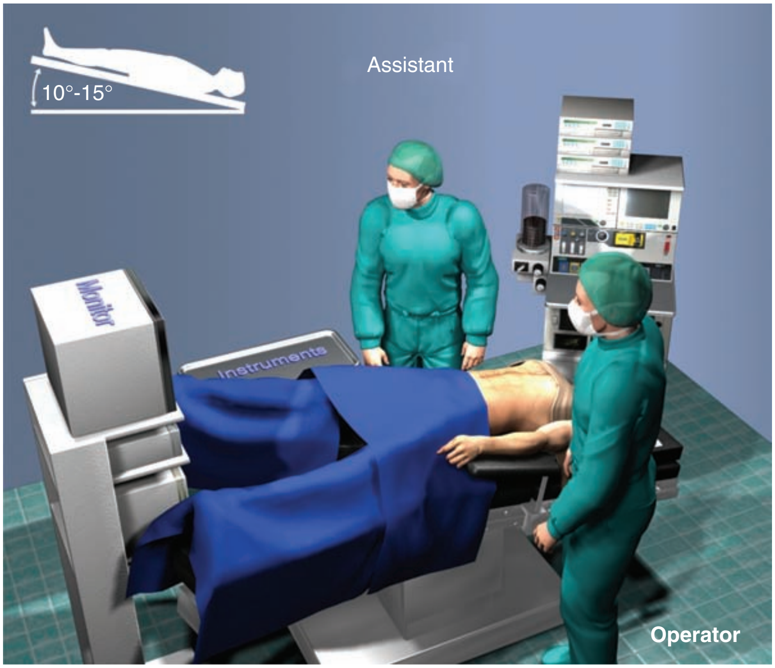

Figure 15.1 Room set-up for endoscopic extraperitoneal radical prostatectomy (EERPE). The camera-holder is positioned behind the patient's head. All have a direct view on the monitor, which is positioned between the straddled legs of the patient.

of the patient's dislocation during the procedure. The left arm is accessible to the anesthesiologist and the intravenous cannulas are herein inserted, while the right arm is draped adherent to the patient's body.

Creation of the preperitoneal space and trocar placement

The first step in the procedure is to create a preperitoneal space. A 15 mm incision is made in the infraumbilical crease immediately lateral to the midline and carried down to the anterior rectus fascia. The anterior rectus fascia is horizontally incised, exposing the rectus muscle. The rectus muscle fibers are vertically separated by blunt dissection, exposing the posterior rectus fascia. The space between the rectus muscle and the posterior rectus sheath is bluntly developed by finger dissection in the direction of the preperitoneal space (Figure 15.2A). The posterior rectus sheath is absent inferior to the arcuate line. A balloon trocar is introduced superior to the posterior rectus sheath and insufflated under direct visual control (Figure 15.2B). The epigastric vessels and the pubic arch are the main landmarks during balloon dilation. The balloon trocar is removed and stay sutures are then placed on either end of the anterior rectus sheath incision. An optical trocar (Hassan type) is introduced and fixed. After insufflation with CO_2 (12 mmHg), the second 5 mm trocar is positioned 2 fingertips left, lateral to the midline (at a 1/3 to 2/3 ratio from the umbilicus

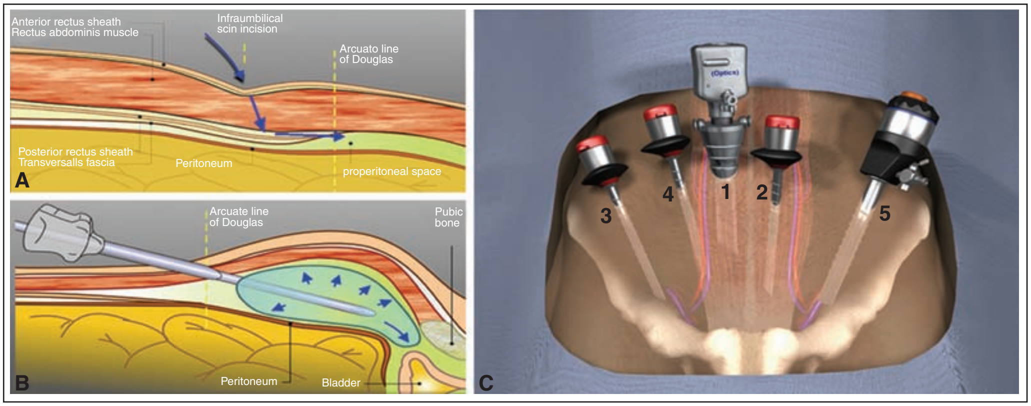

Figure 15.2 Dissection of the preperitoneal space and trocar placement. (A) Landmarks for the dissection of the preperitoneal space. The space between the rectus muscle and the posterior rectus sheath is first of all bluntly developed by finger dissection. (B) Balloon trocar insertion and insufflation, creating the retroperitoneal working space under direct visual control. (C) Trocar placement for EERPE (sequence of placement of trocars for EERPE). Notice the course of the epigastric vessels on both sides.

to the pubic arch). Furthermore, a 5 mm trocar is then positioned medial to the right anterior superior iliac spine. Another 5 mm trocar is placed in the right pararectal line, taking care to avoid injury to the epigastric vessels. The left preperitoneal space is bluntly dissected from the right side. The final 12 mm trocar is placed approximately 3 fingerbreadths medial to the left anterior superior iliac spine (Figure 15.2C). In extremely obese or very tall patients, all trocars should be placed 1–3 cm caudally for optimal access to the retropubic space.

Pelvic lymph node dissection

Pelvic lymph node dissection is performed, including lymph nodes pertaining to the area between the bifurcation of the common iliac artery (cranial border), the iliac vessels and spermatic cord (lateral border), the pubic bone (caudal border), and the obturator nerve (posterior border).

Bladder neck dissection

The anterior surface of the bladder neck and prostate and the endopelvic fascia are exposed and the fatty tissue overlying these structures is gently swept away. The superficial branch of the deep dorsal vein complex is fulgurated with bipolar forceps and divided. The endopelvic fascia is not incised and the Santorini plexus is not ligated at the beginning of the procedure in intrafascial nerve-sparing EERPE as performed in ‘wide excision’ EERPE[10] and ‘classical’ nerve-sparing EERPE.[13] The bladder neck can be identified after the removal of all adherent perivesicular fatty tissue that overlaps the prostate in the shape of a triangle. The dissection starts at the 12 o’clock position at the tip of this triangle. The incision of the bladder neck is enlarged from the 10 to the 2 o’clock position, and the longitudinal musculature of the bladder neck is developed (Figure 15.3 [inset]).

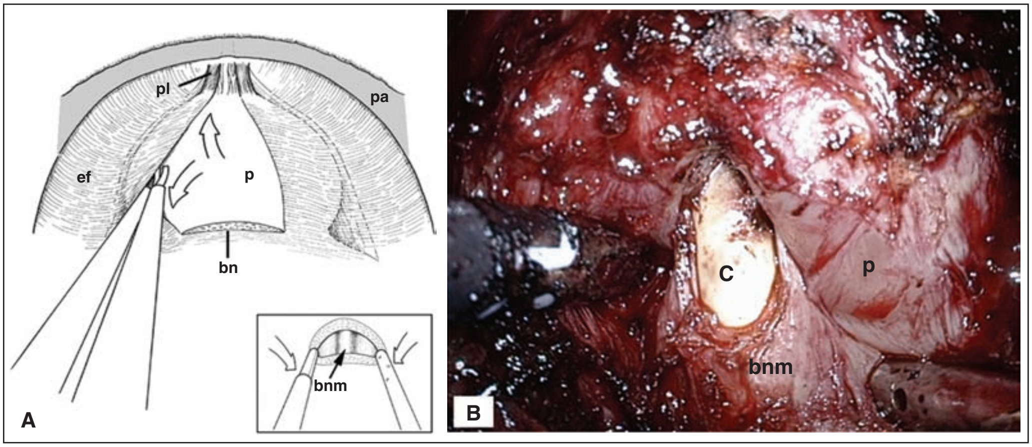

Figure 15.3 Anterior bladder neck dissection. The incision of the bladder neck is performed from the 10 to the 2 o'clock positions, and the longitudinal musculature of the bladder neck is developed (inset). In intrafascial nerve-sparing procedures, it is important to incise the thin fascia overlaying the anterior aspect of the prostate sharply toward the apex medially to the puboprostatic ligaments to create the landmarks for further dissection (A). After incision of the longitudinal musculature of the bladder neck, the bladder–catheter becomes visible (B). It is pulled up into the retropubic space by the assistant under continuous tension to guide further bladder neck dissection. Key: p = prostate, pa = pubic arc, pl = puboprostatic ligament, bn = bladder neck, bnm = bladder neck musculature, ef = endopelvic fascia, c = catheter.

In intrafascial nerve-sparing procedures, it is important to incise the thin fascia overlaying the anterior aspect of the prostate sharply toward the apex medially to the puboprostatic ligaments (Figure 15.3A) to create the landmarks where further dissection will be performed later during the procedure. The main goal is to develop the right plane and finally detach the prostate from its 'envelopment', leaving intact the puboprostatic ligaments, the periprostatic fascia, and the endopelvic fascia as a continuous structure.

The bladder neck is now completely incised and the deflated balloon–catheter becomes visible (Figure 15.3B). It is pulled up into the retropubic space by the assistant under continuous tension. The dissection is now continued in the lateral direction, in the plane between bladder neck and prostate, taking care not to involve the lateral tissue attachments of the prostate and bladder.

Then, the posterior bladder neck is completely dissected. Care is taken to carry down the dissection in the correct plane between the prostate and the bladder neck in order to avoid any intraprostatic perforation. The bladder neck is first completely divided between the 5 and 7 o'clock positions. The ampullary portions of the vas deferentia are visualized as anatomical landmarks (Figure 15.4). The dissection is extended bilaterally.

Dissection of the seminal vesicles

After the division of the vas, the seminal vesicles are freed. It is very important for the assistant to exert contralateral traction on the vas with the forceps in his right hand, and to

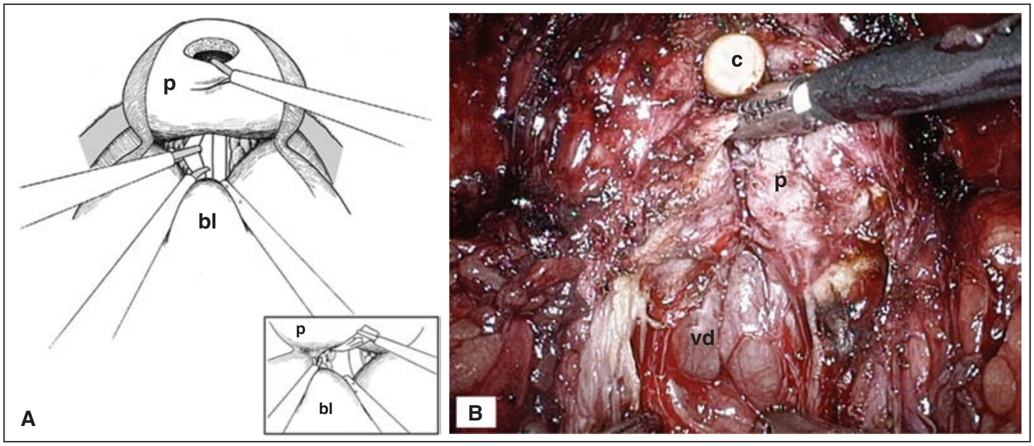

Figure 15.4 Posterior bladder neck dissection. The posterior bladder neck is first completely divided between the 5 and 7 o'clock positions. The ampullary portions of the vas deferentia have to be visualized as anatomical landmarks (B) and divided (A). The dissection is then extended bilaterally (inset). Key: p = prostate, bl = bladder, vd = vas deferentia, c = catheter.

push the bladder down with the instrument in his left hand (Figure 15.4 [inset]). After completion of seminal vesicle dissection, both the surgeon and the assistant retract the seminal vesicles in a craniolateral direction, exposing the posterior layer of Denonvilliers' fascia. In contrast to our previously described technique we do not incise the fascia. The desired plane of dissection is between Denonvilliers' fascia and the prostatic capsule, as shown in the Figure 15.5. The appropriate plane is found by blunt dissection and by stripping down Denonvilliers' fascia from the prostatic capsule (most cases). Complete mobilization of Denonvilliers' fascia and all adhesive tissue is performed on the posterior surface of the prostatic capsule to gain medial access to the prostatic pedicle and neurovascular bundles.

When such dissection is not possible, a small incision can be performed to facilitate the process (Figure 15.5 [inset]). In that case you will be able to see the prerectal fatty tissue. The mobilization of the periprostatic fascia from the prostatic capsule is continued, by blunt and sharp dissection, in order to get lateral access to the prostatic pedicles and the neurovascular bundles. For this step the prostate must be pushed laterally by the assistant.

Prostatic pedicle dissection and sparing of the neurovascular bundles

The prostatic pedicle must now be meticulously divided with the aid of the UltraCision or SonoSurg devices. During dissection of the left prostatic pedicle, the assistant retracts the partially mobilized prostate to the right side, and vice versa. The main parts of the neurovascular bundles are attached to the dorsolateral surface of the prostate. Using the UltraCision or SonoSurg devices, the neurovascular bundles are completely separated from the prostate during prostatic pedicle dissection. The device is mostly used as a dissecting tool and only when absolutely necessary thermal energy is activated. Alternatively, the prostatic pedicle and small vessels can be clipped and divided between endoclips (Figure 15.6). Care has to be

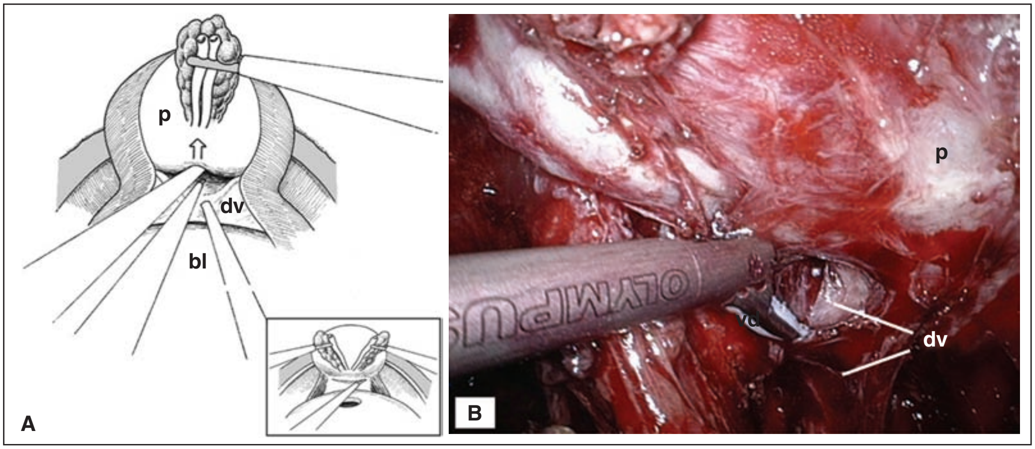

Figure 15.5 Dissection of Denonvilliers' fascia. After completion of seminal vesicle dissection, the desired plane of dissection is between Denonvilliers' fascia and the prostatic capsule (A and B). The appropriate plane is found by stripping down Denonvilliers' fascia from the prostatic capsule (most cases). When such dissection is not possible, a small incision can be performed to facilitate the process (inset). Key: p = prostate, bl = bladder, dv = Denonvilliers' fascia.

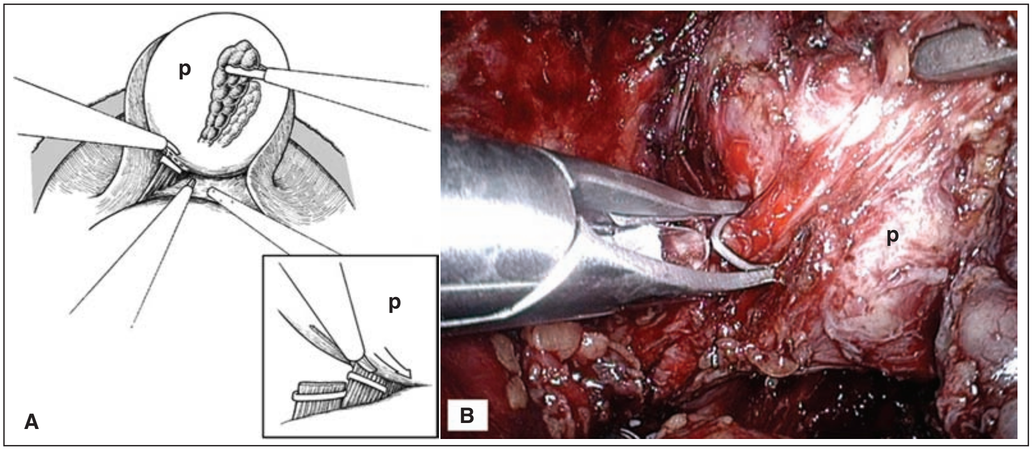

Figure 15.6 Prostatic pedicle dissection. During dissection of the left prostatic pedicle, the assistant retracts the partially mobilized prostate to the right side (A), and vice versa. The prostatic pedicle and small vessels are clipped and divided between endoclips (B). Care has to be taken to avoid inadvertent injury to the neurovascular bundle. It is advisable to proceed with clipping and cutting in small steps (inset). Key: p = prostate.

taken to avoid inadvertent injury to the neurovascular bundle. It is advisable to proceed with clipping and cutting in small steps.

Having made an incision in the thin fascia overlaying the anterior aspect of the prostate at the beginning of the procedure and the posterior dissection between Denonvilliers' fascia and prostatic capsule, we have two safe planes for the intrafascial nerve-sparing procedure. The 'shining' surface of the prostatic capsule is clearly seen laterally as well as posteriorly (Figure 15.7). The periprostatic fascia and the neurovascular bundle can be separated from the prostatic capsula by blunt dissection in most cases.

The preservation of the neurovascular bundles close to the apex of the prostate is performed anterolaterally. The assistant pulls the prostate to the right side for preparation of the left neurovascular bundle and vice versa.

Santorini plexus ligation

The ligation is performed and after the prostate is pushed into the pelvis contralaterally to provide good access to the apex and the urethra. The mobilized puboprostatic ligaments and the remaining puboprostatic fascia on the lateral surface of the prostate are now completely detached from the urethra and the apex. The Santorini plexus is ligated with a 2/0-Vicryl (polyglactin) on a CT-1 needle (slightly bent upward) by selective passage of the needle

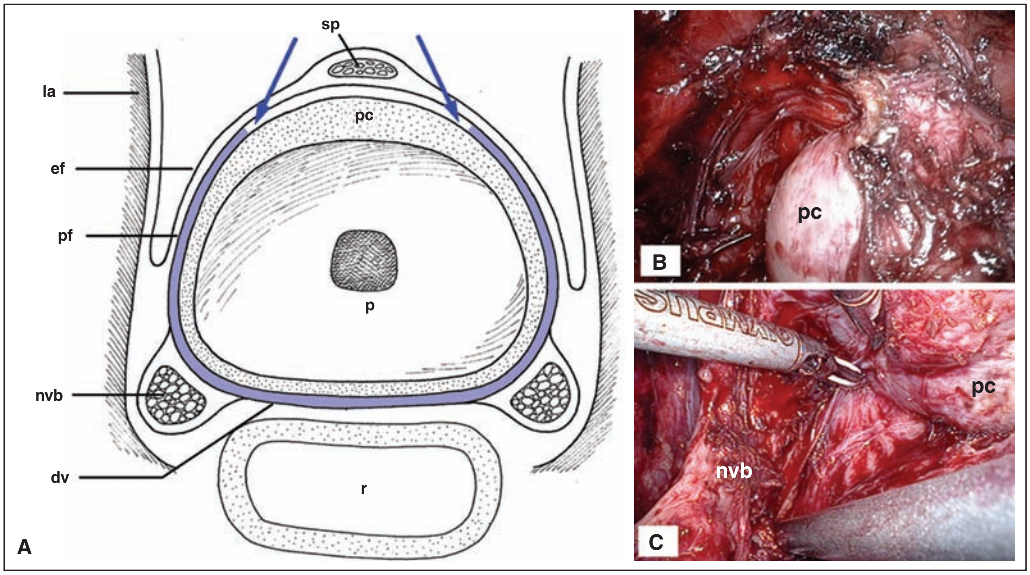

Figure 15.7 Intrafascial preservation of the neurovascular bundles. Schematic depiction of cross section through prostate to show anatomical relations of prostate, endopelvic fascia, periprostatic fascia, Denonvilliers' fascia, and neurovascular bundles (A). Dissection plane for intrafascial nerve sparing is shown in blue (arrows). The 'shining' surface of the prostatic capsula is clearly seen laterally (B) as well as posteriorly (C). The periprostatic fascia and the neurovascular bundle can be separated from the prostatic capsula by blunt dissection in most cases. Key: p = prostate, la = levator ani muscle, nvb = neurovascular bundles, sp = Santorini plexus, pc = prostatic capsule, ef = endopelvic fascia, pf = periprostatic fascia, dv = Denonvilliers' fascia, r = rectum.

underneath the plexus from left to right. During this step the assistant pushes the prostate dorsocranially to elongate the urethra.

Apical dissection

The next step – the apical dissection – is a three-step procedure. The Santorini plexus and overlying connective and areolar tissue is initially dissected. Then, the junction between urethral sphincter (striated and smooth muscular components) is dissected. Finally, the inner smooth muscular layer of the urethra is freed and dissected (Figure 15.8). As soon as the urethral catheter becomes visible, the assistant retracts the catheter towards the symphisis. The verumontanum is now clearly visible. The dissection of the posterior urethra starts distally to the verumontanum. The final detachment of the posterior urethra is performed dorsolaterally to avoid any injury to the neurovascular bundles and the rectum. The assistant retracts the seminal vesicle controlaterally out of the pelvis and also pushes the prostate dorsolaterally.

When the prostate is completely dissected from its adjacent structures, it is then placed in an endoscopic retrieval bag. The bag containing the prostatic specimen is partly extracted through the trocar site and clamped with a Kocher clamp. The trocar is then repositioned parallel to the bag, which is located in the left iliac fossa.

Urethrovesical anastomosis (interrupted sutures)

The anastomosis is performed with 9 interrupted 2-0 Vicryl sutures with a UR-6 needle. All stitches are made ‘outside-in’ at the bladder neck and ‘inside-out’ at the urethra. In this way, the sutures are always tied extraluminally (Figure 15.9).

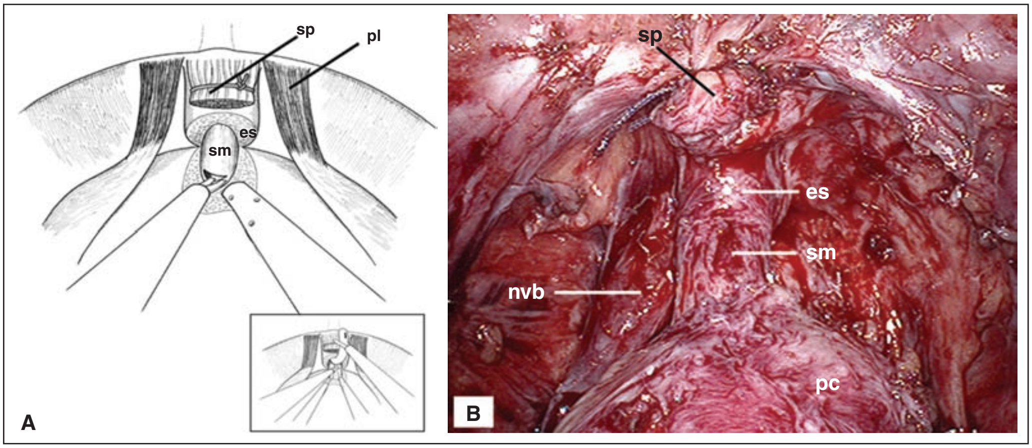

Figure 15.8 Apical dissection. The apical dissection is a three-step procedure. The Santorini plexus is initially dissected. Then the junction between external (urethral) sphincter is dissected. Finally, the inner smooth muscular layer of the urethra is freed (B). As soon as this layer is incised, the urethral catheter becomes visible (A). The assistant retracts the catheter towards the symphysis (inset) to guide the dissection of the posterior urethra distally to the verumontanum. Key: pc = prostatic capsule, nvb = neurovascular bundle, sp = Santorini plexus, pl = puboprostatic ligament, es = external (urethral) sphincter, sm = inner longitudinal smooth muscular layer of the urethra.

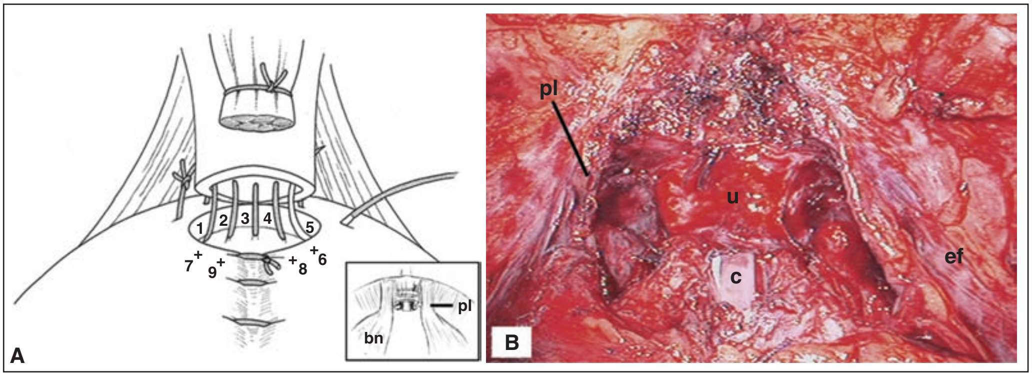

Figure 15.9 Urethrovesical anastomosis (interrupted sutures, 2-0 Vicryl, UR-6 needle). The stitches are always made ‘outside-in’ at the bladder neck and ‘inside-out’ at the urethra and always tied extraluminally. The exact position of all stitches is seen in (A) (numbers 1–9 = sequence of placement). If necessary, the bladder neck is reconstructed at the 12 o’clock position, prior to the finalization of the anastomosis. If the dorsal part of the anastomosis has been concluded in intrafascial nerve-sparing EERPE (inset), the puboprostatic ligaments, the intact endopelvic fascia, the urethra, the bladder neck, and the catheter are clearly visible (B). Key: pc = prostatic capsule, ef = endopelvic fascia, bn = bladder neck, u = urethra, c = catheter.

The first stitch starts at the 8 o’clock position (backhand–backhand), followed by stitches at the 7, 6, and 5 o’clock positions (forehand at the bladder neck, backhand at the urethra). After each urethral stitch, the catheter needs to be pulled back in order to rule out fixation by the anastomotic suture. The 4 o’clock stitch is then done forehand (bladder neck)–forehand (urethra). After the dorsal circumference has been completed, the catheter is placed into the bladder and the anastomosis is completed anterolaterally and ventrally. On the left side, the stitches are thrown backhand–backhand and on the right side forehand–forehand.

If during the bladder neck-dissection a bladder neck-preserving technique is not feasible, bladder neck reconstruction is deemed necessary at the 12 o’clock position, before the two final stitches at the 11 and 1 o’clock positions are placed. The watertightness of the anastomosis is finally checked by filling the bladder with 200 ml of sterile water.

Concomitant hernia repair

In approximately 8% of patients operated on with EERPE, there is a need for a concomitant repair of unilateral or bilateral inguinal hernia repair. In these cases, we perform a standardized totally extraperitoneal hernia repair technique, which uses the principle of tension-free hernia repair, overlaying the entire myopectineal orifice with one large piece of mesh. The mesh is 10 × 15 cm; it is incised in the middle and a small hole cut into the mesh to provide sufficient space for the spermatic cord. The split within the mesh is covered by a flap (6 × 5 cm). The main goal of this technique is to elevate the spermatic cord at the side of the inguinal hernia defect, place the prepared polypropylene mesh around the spermatic cord, and finally cover the hernial orifices and the entire space from the symphysis pubis in the midline to the abdominal wall laterally (Figure 15.10). No staples or sutures are necessary

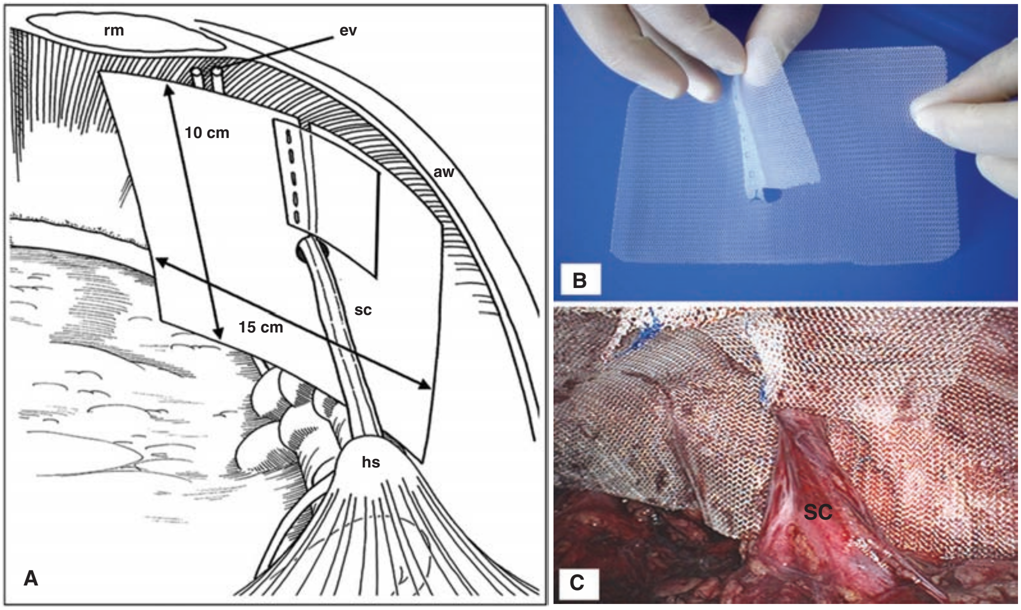

Figure 15.10 Concomitant inguinal hernia repair. In the case of a concomitant inguinal hernia, a 10 × 15 cm polypropylene mesh is placed in the preperitoneal space covering both direct and indirect hernial orifices at the end of the prostatectomy (A). The mesh is prepared extracorporally (B). It is incised in the middle and a small hole cut into the mesh is made to provide sufficient space for the spermatic cord. The split within the mesh is covered by a flap. The polypropylene mesh is placed around the spermatic cord (C). Therefore, no staples or sutures are necessary to fix the mesh. Key: sc = spermatic cord, hs = hernia sac, ev = epigastric vessels, rm = rectus muscle, aw = abdominal wall musculature.

for fixing the mesh; the mesh is anchored and fixed to the abdominal wall by intra-abdominal pressure alone.[22] Closing the peritoneal defect (if there is one) after placing the mesh is essential to avoid exposing the mesh to the intra-abdominal organs. Direct contact of the mesh with the bowel must be avoided.

Placement of drainage and postoperative care

At the end of the procedure, a 16F Robinson drainage catheter is placed into the retropubic space. Finally, the endoscopic bag containing the specimen is retracted through the 12 mm trocar site at the end of the procedure. The drain is removed 24–48 hours after the procedure. Five days postoperatively, a cystogram is performed and if there is no anastomotic leak the urethral catheter is removed.

SUMMARY

EERPE is a further advancement of minimal invasive surgery as it overcomes the limitations of LRPE by the strictly extraperitoneal route of access, combining the advantages of minimal invasive surgery with the advantages of an extraperitoneal procedure. Today, our experience is based on a series of 1500 patients who underwent minimally invasive radical prostatectomy using this entirely extraperitoneal retropubic approach. In this chapter we have presented our technique of intrafascial nsEERPE. This modification of 'classical' nerve-sparing prostatectomy keeps the endopelvic fascia intact and maintains the puboprostatic ligaments. In addition, the anterior approach to the periprostatic fascia enables a less traumatic dissection from the prostate and thus a more viable neurovascular bundle.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the assistance of Mr Jens Mondry (Director Moonsoft, Germany) in preparing Figures 15.1 and 15.2 and Mr Gottfried Müller in preparing Figures 15.3–15.10.

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Part 5: Robotic-assisted radical prostatectomy

CHAPTER 16

A transition from open to robot-assisted laparoscopic prostatectomy: the Vanderbilt experience

Joseph A Smith Jr and S Duke Herrell

Despite a proliferation of new technologies and treatment options, there seems little reason to believe that surgical removal of the prostate will be displaced in the foreseeable future as the preferred approach for many patients. What is occurring, though, is an almost revolutionary shift in the surgical approach for radical prostatectomy. In only a few short years, laparoscopic prostatectomy with or without robotic assistance has emerged as a preferred alternative for many patients undergoing radical prostatectomy, and it seems likely that it will become the dominant surgical approach in only a short time.

Important clinical outcomes after radical prostatectomy correlate directly with surgeon experience. Virtually all studies have shown a lower rate of positive margins and decreased complications for highly experienced vs novice surgeons, regardless of surgical approach. This recognition places a burden upon a surgeon experienced with open radical prostatectomy who wants to make a transition to a laparoscopic approach.

This chapter reviews our experience with radical prostatectomy at Vanderbilt University Medical Center. In particular, we discuss lessons learned in making a transition from a practice dominated by radical retropubic prostatectomy (RRP) to a high-volume robot-assisted laparoscopic prostatectomy program. The merits of each approach and the comparative outcomes are presented, along with the requisite and recommended training steps for the individual surgeon as well as the program.

WHY PERFORM ROBOT-ASSISTED LAPAROSCOPIC PROSTATECTOMY?

It would be naive to ignore the fact that marketing by individuals, hospitals, and industry is one of the primary driving forces behind the proliferation of robot-assisted laparoscopic prostatectomy. Virtually every hospital that acquires a robotic system launches a campaign to announce the acquisition of this state-of-the-art technology and to extol the many advantages of this surgical approach. Websites are carefully crafted to advertise robotic surgery and recruit patients. Over and above this, though, there are legitimate patient advantages that have been consistently demonstrated with robot-assisted laparoscopic prostatectomy.

Technically adept laparoscopic surgeons question whether the robotic instrumentation adds any meaningful value to the procedure. For those with sufficient laparoscopic technical proficiency, the robot may not be required or, even, advantageous. For the overwhelming majority of surgeons, though, robotic assistance makes the surgical dissection easier and greatly facilitates suturing. Certainly, the transition from open to laparoscopic surgery is greatly eased by the surgical robot.

Aside from patient demands, the primary motivating factor for performance of robot-assisted laparoscopic prostatectomy (RALP) is improvement in surgical outcomes. Comparative outcomes are discussed below. However, it is evident from our series, as well as others, that at least comparable outcomes can be achieved in all measures and there is demonstrated superiority in some. These improved outcomes serve as the primary basis for the establishment and further development of RALP.

TECHNICAL ASPECTS

As with open surgery, various nuances in surgical approach for RALP have been described. The following technique is based upon our own experience with over 1000 RALP procedures. Furthermore, it incorporates principles of open radical prostatectomy and lessons learned from an experience with over 3000 RRP operations. We have used exclusively the da Vinci surgical robot (Intuitive Surgical, Sunnyvale, CA). This is a master/slave device wherein the surgeon is seated at a console remote from the operative table. The surgeon is able to control and manipulate the camera as well as three additional robotic arms.

Patient positioning

Proper patient positioning is essential for appropriate exposure of the pelvis and instrument orientation. The patient is placed in a lithotomy position with steep Trendelenburg (Figure 16.1). An egg crate foam pad can help prevent slippage of the patient once the Trendelenburg position is achieved. The Trendelenburg position helps displace bowel from the pelvis when an intraperitoneal approach is used.

The camera port is placed just superior to the umbilicus. Three additional 5 mm ports are placed for the robotic arms and a 12 mm port is placed in the right lower quadrant for the table side assistant. A left upper quadrant port is not necessary in most patients but can be useful as an additional retraction port for the assistant if the colon tends to obscure the pelvis. During most of the dissection, monopolar scissors are used in the right arm with either a grasper or bipolar forceps in the left arm. The fourth arm, which is used for retraction, employs a serrated grasping instrument. The table side assistant provides suction and passage of suture through the right lower quadrant 12 mm port.

Development of the operative field

Both an intraperitoneal and extraperitoneal approach for RALP have been described.[1–3] No distinct differences in outcome have been observed. The extraperitoneal approach helps isolate any urine leak from the peritoneal cavity

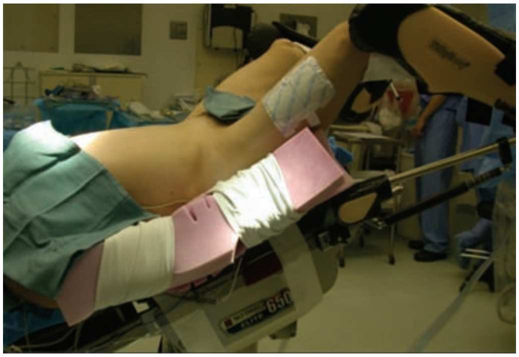


Figure 16.1 Patient positioning for robot-assisted laparoscopic prostatectomy.

and may help with postoperative tamponade of bleeding. However, the working space is smaller and the pneumoperitoneum is lost more easily. As have most surgeons, we have preferred an intraperitoneal approach.

Our initial surgical step is to incise the peritoneum on the lower abdominal wall and carry this laterally and through the median umbilical ligaments. The peritoneal incision then parallels the spermatic cord and deviates medially just distal to the vas deferens. This allows development of the space of Retzius and exposure of the prostate. As with open surgery, careful removal of all the periprostatic fat overlying the prostate improves visualization of key anatomical structures. The superficial dorsal vein can be divided with cautery.

Accessory pudendal arteries are identified in almost 25% of patients (Figure 16.2). With careful dissection, these can almost always be preserved. They may enter the pelvis at different angles but typically will penetrate the genitourinary diaphragm just lateral to the puboprostatic ligament. Preservation of these arteries may be important in avoiding postoperative erectile dysfunction or incontinence.

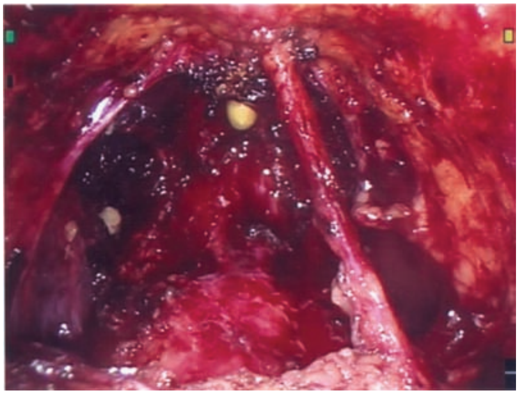


Figure 16.2 A large accessory pudendal artery is visible on the right side. This pierces the genitourinary diaphragm just at the prostatic apex. Identification and preservation of accessory arteries may be important for maintaining penile blood flow and avoiding incontinence and erectile dysfunction.

The endopelvic fascia is incised sharply. An incision too far medial can cause bleeding from the periprostatic veins. The pneumoperitoneum typically limits the bleeding such that specific hemostatic maneuvers are not required. However, if there is substantial bleeding it is best controlled with a figure-of-eight suture. Dissection is performed medially to the level of the puboprostatic ligaments. Further dissection in this area and placement of a suture through the dorsal vein complex are reserved until later in the procedure.

Dissection of the bladder neck

Many surgeons performing RALP describe proper anatomical identification of the bladder neck as one of the most difficult surgical steps. Undoubtedly, this is a key technical maneuver to avoid incision into the prostate or overzealous excision of bladder neck tissue. Some surgeons pull on the inflated Foley catheter to help identify the bladder neck, but this gives only a gross estimation of the proper tissue plane. We have found that careful exposure and visualization of the prostatic contour toward the base permits entry into the proper anatomical plane between the prostate and the bladder neck (Figure 16.3).

A bunching suture on the anterior prostate can help show the contour of the prostatic base. Some of the perivesical fat can be taken down laterally, although veins in this tissue can cause nuisance bleeding. Under magnification, the bladder detrusor muscle has an appearance quite distinct from that of the prostate. The anterior bladder wall is entered, which allows excellent visualization of the posterior bladder neck and trigone. A large median lobe can be grasped with the fourth arm and lifted anteriorly to expose the posterior bladder neck (Figure 16.4). The monopolar scissors are very useful during division of the bladder neck as

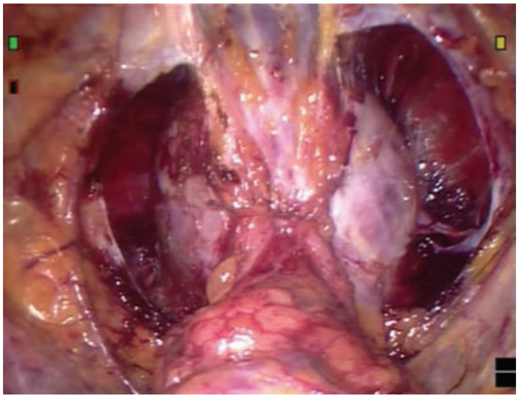


Figure 16.3 The endopelvic fascia has been excised bilaterally. A suture has been placed anteriorly on the prostate to bunch the dorsal vein complex. Removal of some of the perivesical fat allows good visualization of the prostatic contour so that this can be followed at the base to identify the bladder neck.

they typically provide complete hemostasis without causing excessive tissue charring.

A bladder neck incision too far distally risks entry into the prostate and must be corrected by a more proximal incision. If the bladder neck is too patulous, it can be reconfigured with a racket handle closure as described below.

Dissection of the seminal vesicles

The Montsouris technique for isolation of the seminal vesicles involves an initial incision in the peritoneum overlying the pouch of Douglas and identification of the seminal vesicles from that approach.[4] We have preferred dissection and isolation of the seminal vesicles after dividing the posterior bladder neck. An important anatomical landmark is a longitudinal muscle layer which extends from the posterior detrusor to the prostatic base. This muscle layer must be sharply divided to expose the anterior vas deferens and seminal vesicles. The vas deferens is grasped, dissected proximally for a distance, and then divided (Figure 16.5). The distal end of the vas is grasped with the fourth arm, whereas the left arm grasps the proximal vas to allow dissection of the anterior seminal vesicle.

The course of the neurovascular bundle at the base of the prostate and near the seminal vesicles is variable. However, it typically runs

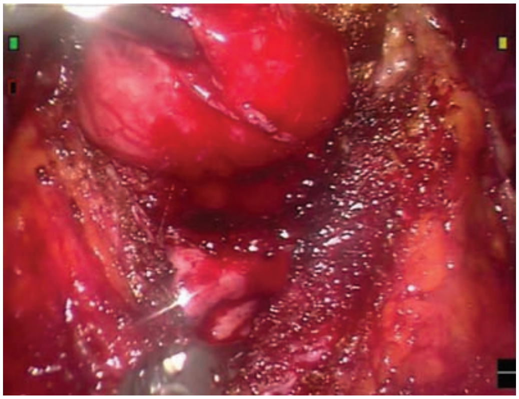


Figure 16.4 The anterior bladder has been incised. The grasper is lifting a large median lobe anteriorly. This allows visualization of the posterior bladder and trigone so that the posterior incision can be made distal to the ureteral orifices.

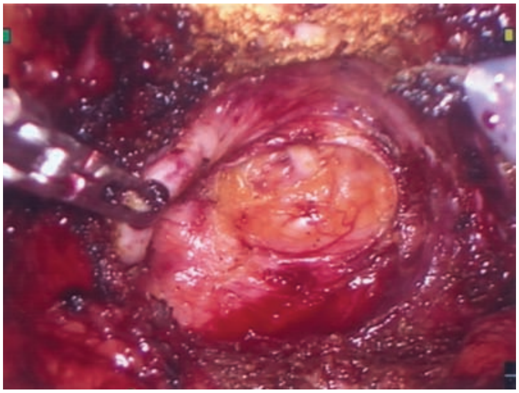


Figure 16.5 The bladder neck has been completely divided, exposing the anterior surface of the seminal vesicles and vasa deferentia. The prostate is being lifted anteriorly. The grasper is holding the left vas deferens.

just posterolateral to the seminal vesicles and is subject to injury during the seminal vesical dissection, especially if excessive cautery is used. The arteries to the seminal vesicle can usually be well visualized and point coagulated. Typically, the entire seminal vesicle is excised. Just as with open surgery, if there is difficulty with exposure, the tip of the seminal vesicle may be left indwelling to help avoid any risk of damage to the neurovascular bundle.

Development of the rectal plane

Most reported series of robot-assisted or pure laparoscopic prostatectomy have included patients with rectal injuries, especially during the early experience. Rectal injury also may occur during RRP. With either approach, intraoperative multilayer closure of the rectum typically prevents postoperative complications, but a pelvic abscess or fistula between the vesicourethral anastomosis and rectum could develop.[5,6] Therefore, appropriate development of the plane between the prostate and rectum is a key step in the surgical approach.

With the antegrade approach characteristically used with RALP, development of the rectal plane is the next surgical step after the seminal vesicles have been dissected free. The seminal vesicles are lifted anteriorly by the fourth arm to expose Denonvilliers' fascia. Complete, sharp incision through Denonvilliers' fascia is important. A surgical approach, sometimes termed 'intrafascial dissection', that leaves Denonvilliers' fascia on the anterior rectal wall, has been described. More suitably, Denonvilliers' fascia should be excised completely along with the prostate, as typically occurs with RRP.

Once Denonvilliers' fascia is incised, the prerectal fat is readily visualized (Figure 16.6). The rectum is mobilized off of the posterior portion of the prostate as far distally and laterally as vision permits. Complete mobilization in this manner allows the rectum to drop posteriorly at the prostatic apex such that rectal injury can be avoided when the urethra is divided.

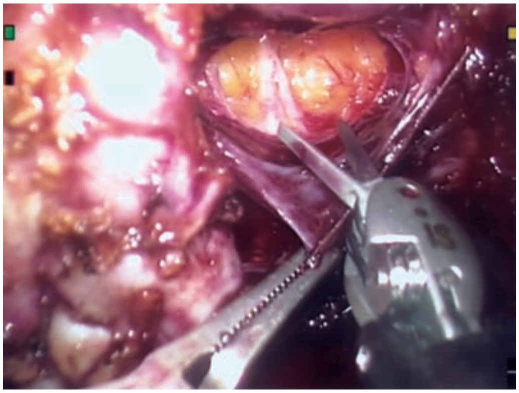


Figure 16.6 The vasa deferentia and seminal vesicles have been dissected free and are being lifted anteriorly. The grasper is holding Denonvilliers' fascia, which has been incised. The exposed fat lies just anterior to the rectum.

Control of the vascular pedicle

Again, various methods are described for control of the vascular pedicle during RALP. Simple division using monopolar instruments or bipolar cautery have been described. Some surgeons use temporary occlusion with bulldog clamps and others use placement of hemostatic sutures. We have preferred locking clips, as this avoids use of any thermal energy and provides secure hemostasis.

A key step in appropriate placement of the clips is appropriate isolation of the pedicle. This is facilitated by mobilization of the rectum and complete division of the bladder neck. The location of the neurovascular bundle along the lateral prostate must be determined prior to placement of the clips (Figure 16.7). When the pedicle is well-isolated, two clips per side usually are sufficient to provide complete pedicle control. The clips should be placed far enough away from the prostate that a sharp

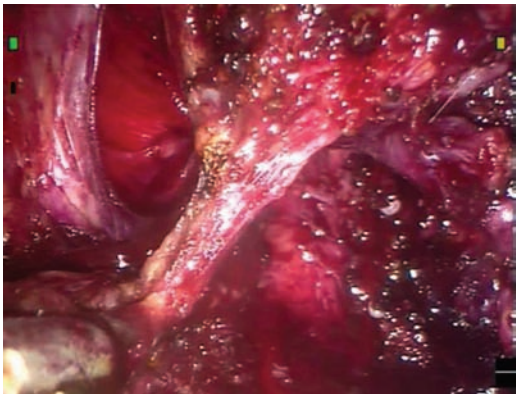


Figure 16.7 The left prostatic pedicle is isolated so that the vessels can be controlled with hemoclips. The prostate gland is lifted anteriorly and to the right. The preserved neurovascular bundle is visible just lateral to the pedicle.

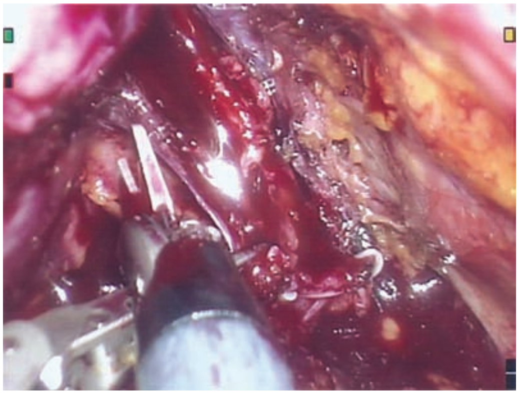


Figure 16.8 The neurovascular bundle is being separated from the right side of the prostate. The robotic scissors are being used to develop this plane and cautery energy is avoided.

incision can be made between the clip and the prostate itself. Improper placement too far laterally or distally risks damage to the neurovascular bundle.

Dissection of the neurovascular bundle

The applicable surgical principles for release of the neurovascular bundle from the prostate are identical irrespective of whether an open or laparoscopic approach is used. Thermal damage and traction injury must be avoided in either case.[7] The limited bleeding associated with RALP facilitates identification and dissection of the neurovascular bundle. On the other hand, a relatively small amount of bleeding can obscure the operative field with magnification.

Dissection begins along the lateral prostate at about the midportion. It is at this point that the prostatic fascia separates most readily from the capsule. The dissection continues distally to the apex to release the bundle completely at that point (Figure 16.8). Visualization of the bundle itself is difficult near the pedicle but, with isolation and division of the pedicle as described previously, the bundle falls posterolaterally away from the prostate.

Most of the small blood vessels encountered during the dissection do not require specific hemostatic measures. Periodic suctioning to clear the operative field is typically sufficient. If a larger vessel is visualized, it can be point coagulated or sutured. Small clips may be used if a larger vessel coursing from the neurovascular bundle to the prostate is visualized. The bundle is released completely from the posterolateral prostate, which allows the prostate to be elevated such that the only remaining attachments are the puboprostatic ligaments, the dorsal vein complex, and the urethra.

The apical dissection

As with open surgery, one of the key aspects of RALP is the apical dissection. This is crucial not only in avoiding incontinence and erectile dysfunction but also because the apex is the most common site for positive margins. RALP typically provides excellent visualization of the prostatic apex (Figure 16.9).

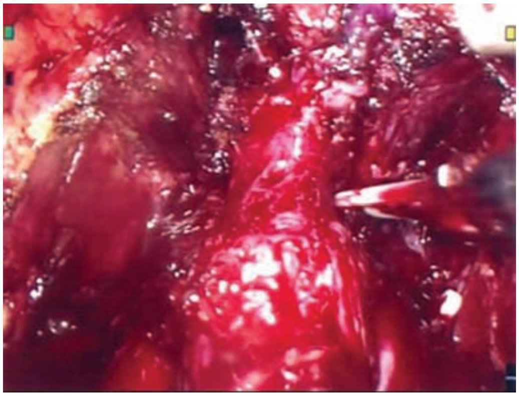


Figure 16.9 The dorsal vein complex has been divided, exposing the prostatic apex and the urethra.

There are different ways to control the deep dorsal vein complex. Some surgeons prefer using a stapling device while others simply use bipolar cautery. As with open surgery, we prefer a carefully placed hemostatic suture. The puboprostatic ligaments are partially incised to visualize better the prostatic apex. A figure-of-eight 0 Vicryl (polyglactin) suture is placed through the dorsal vein complex and secured. Shaving of the anterior prostatic apex can occur in an effort to leave sufficient length on the dorsal vein complex. Thus, it is important to divide the complex immediately adjacent to the suture. If the suture becomes dislodged, it can be easily replaced. We have found that progressive dissection along the right and left margins of the prostate can help further define the urethra and use this maneuver both for open surgery and RALP. With this progressive dissection, the only remaining attachment is the urethra, which is divided 0.5 cm distal to the prostatic apex. The surgical specimen is then placed in a laparoscopy entrapment bag (Figure 16.10).

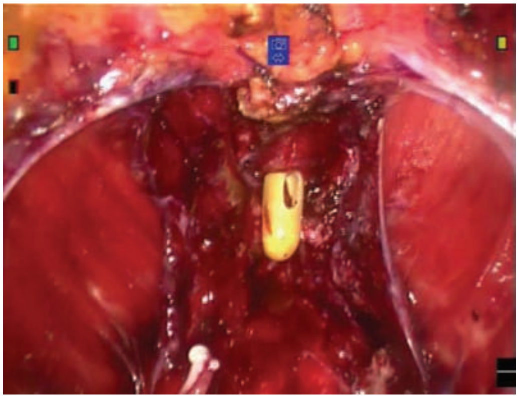


Figure 16.10 The prostate has been removed and placed in an entrapment bag. The catheter tip shows the cut urethra and the clips on the pedicle are seen. The preserved neurovascular bundles are visible bilaterally.

The vesicourethral anastomosis

One of the primary advantages of robotic assistance with laparoscopic prostatectomy is the improved ability to place anastomotic sutures. Again, different techniques have been described but most use a running, single-knot absorbable suture (Figure 16.11). Good tissue bites are important on the posterior bladder and there is usually more than sufficient room distal to

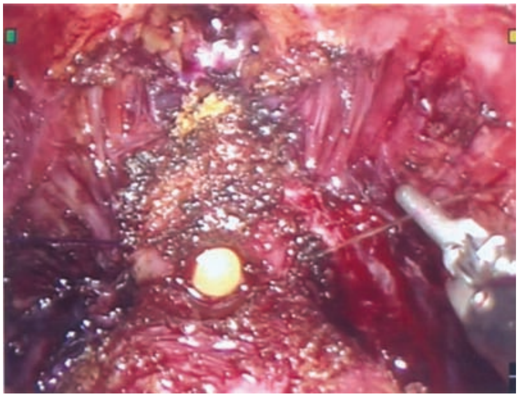


Figure 16.11 A running, single-knot suture is used for the anastomosis. The sutures have been partially placed and careful tension on the sutures approximates the posterior bladder neck to the urethra.

the trigone to permit this. The posterior urethral bite should avoid excessive accordion-like compression of the urethra but should incorporate sufficient periurethral tissue so that there is adequate strength as the sutures are laced together. Each suture is run anteriorly and tied at that point. If the bladder neck is too large, we prefer to perform an anterior racket handle closure. This allows the posterior bladder to be approximated directly to the urethra without tension and the racket handle closure is easily visualized. A catheter is then passed through the anastomosis and a drain placed in the left lower quadrant through one of the robot port sites.

PERIOPERATIVE CARE

We use the same evidence-based pathway for perioperative patient management, regardless of whether an open or laparoscopic procedure is performed (Figure 16.12). The care pathway is designed for the ideal patient, and postoperative laboratory studies and other interventions are limited. This streamlines care, reduces variability, and can decrease both patient morbidity and hospital costs. However, it does not diminish the physician's role or responsibility for oversight of postoperative care. The physician must recognize situations in which deviations from the pathway are indicated.

The only difference in our pathway is in the use of perioperative anticoagulation. With RRP, low molecular weight heparin is administered preoperatively and continued for 24 hours. We do not routinely use any anticoagulation in the RALP group. The risk of thromboembolic complications seems to be lower with laparoscopic surgery. Furthermore, there are concerns that the intraperitoneal operative field may not permit effective tamponade of any postoperative bleeding.

Since our pathways are otherwise identical, many of the comparative outcome measures are, likewise, no different. Discussed below are our results for various immediate and longer-term patient outcomes.

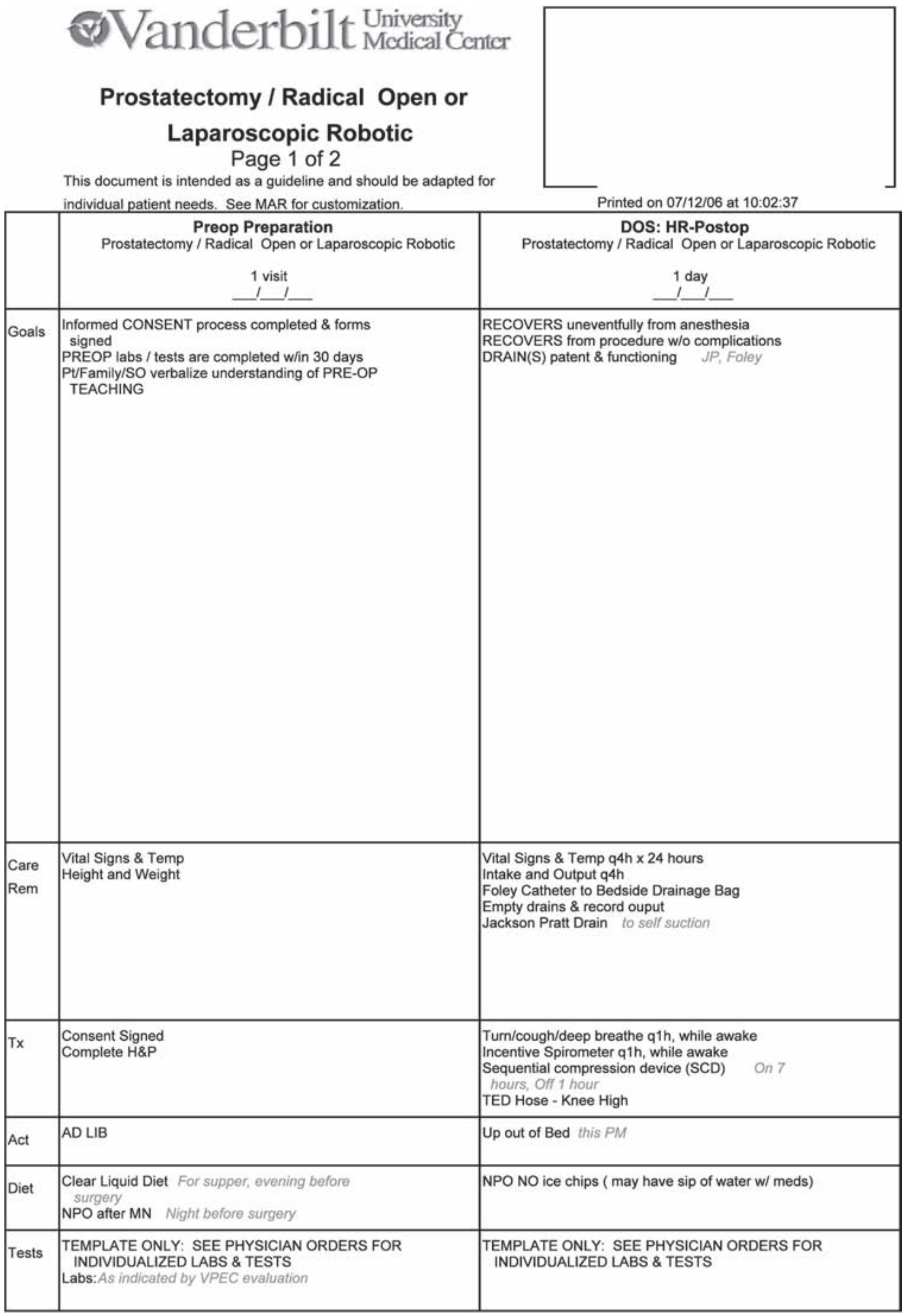
Intraoperative bleeding

Because of the rich venous plexus which surrounds the prostate, radical prostatectomy is an operation with the potential for significant bleeding. Pressure from the pneumoperitoneum compresses venous bleeding during RALP and contributes significantly to the minimal blood loss typically associated with the procedure. Virtually every study has shown a lower blood loss associated with RALP compared to RRP. Our own results confirm this.[8] The median discharge hematocrit for patients undergoing RALP is 38% compared with 33% in those undergoing retropubic prostatomy (p <0.05).

The most significant factor for patients undergoing radical prostatectomy, though, is not the average blood loss; rather, it is the proportion of patients who exceed a certain threshold for blood loss wherein transfusion of blood products is required. Depending upon circumstances, blood loss which exceeds 1500 cc usually requires replacement with blood products. We typically have not recommended that patients donate autologous blood preoperatively. In our prospective comparative series, 3% of patients undergoing RRP have required administration of homologous transfusion compared with fewer than 1% with RALP. It is recognized that this transfusion requirement is lower than many reported series for open surgery and this affects the comparative results.

Postoperative pain

Pain is not characteristically a prominent feature in patients recovering from radical prostatectomy, regardless of surgical approach. Pain from the relatively limited infraumbilical



Vanderbilt University Medical Center

Prostatectomy / Radical Open or Laparoscopic Robotic

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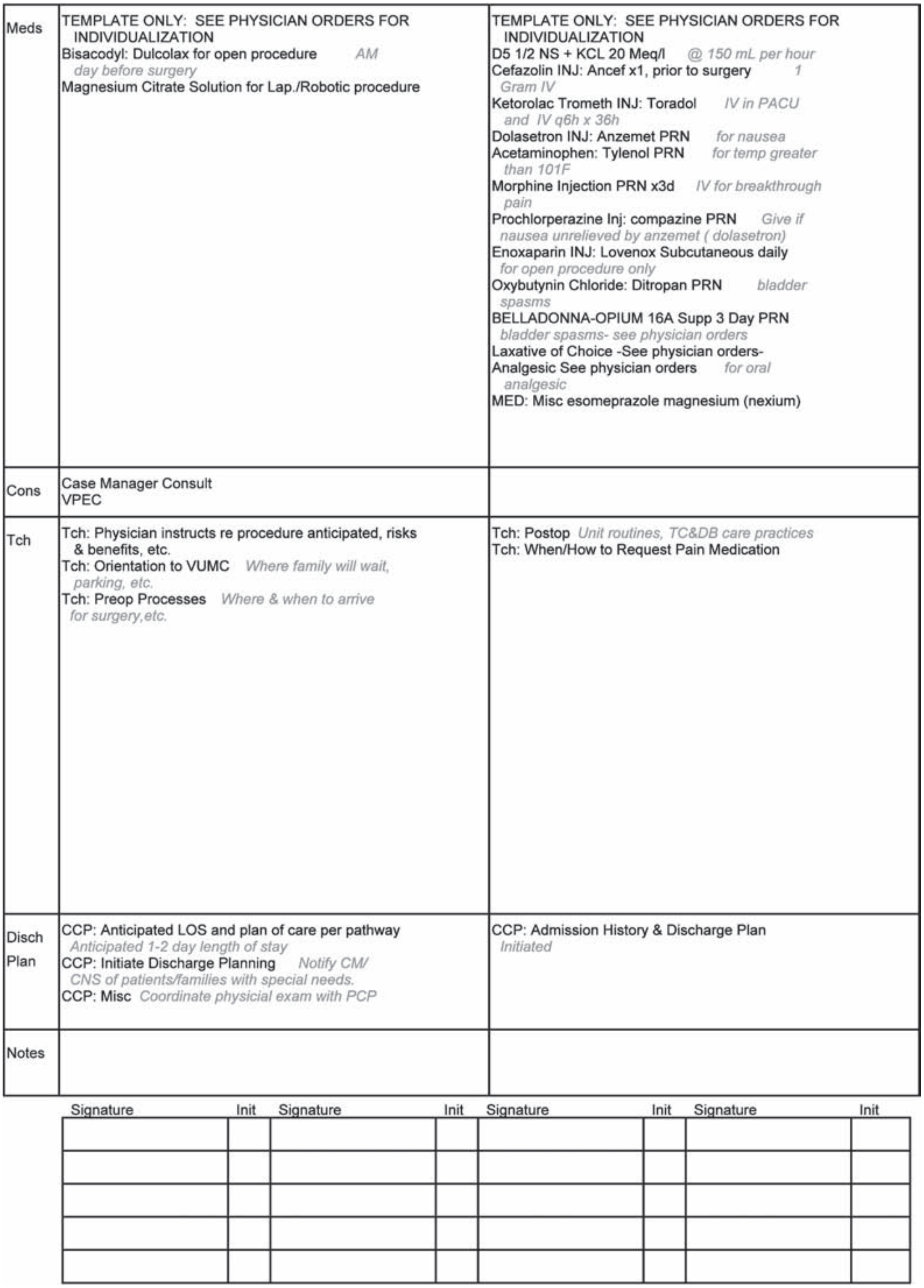
	Preop Preparation Prostatectomy / Radical Open or Laparoscopic Robotic 1 visit ___/___/___	**DOS: HR-Postop** Prostatectomy / Radical Open or Laparoscopic Robotic 1 day ___/___/___
Goals	Informed CONSENT process completed & forms signed PREOP labs / tests are completed w/in 30 days Pt/Family/SO verbalize understanding of PRE-OP TEACHING	RECOVERS uneventfully from anesthesia RECOVERS from procedure w/o complications DRAIN(S) patent & functioning *JP, Foley*
Care Rem	Vital Signs & Temp Height and Weight	Vital Signs & Temp q4h x 24 hours Intake and Output q4h Foley Catheter to Bedside Drainage Bag Empty drains & record ouput Jackson Pratt Drain *to self suction*
Tx	Consent Signed Complete H&P	Turn/cough/deep breathe q1h, while awake Incentive Spirometer q1h, while awake Sequential compression device (SCD) *On 7 hours, Off 1 hour* TED Hose - Knee High
Act	AD LIB	Up out of Bed *this PM*
Diet	Clear Liquid Diet *For supper, evening before surgery* NPO after MN *Night before surgery*	NPO NO ice chips (may have sip of water w/ meds)
Tests	TEMPLATE ONLY: SEE PHYSICIAN ORDERS FOR INDIVIDUALIZED LABS & TESTS Labs:*As indicated by VPEC evaluation*	TEMPLATE ONLY: SEE PHYSICIAN ORDERS FOR INDIVIDUALIZED LABS & TESTS

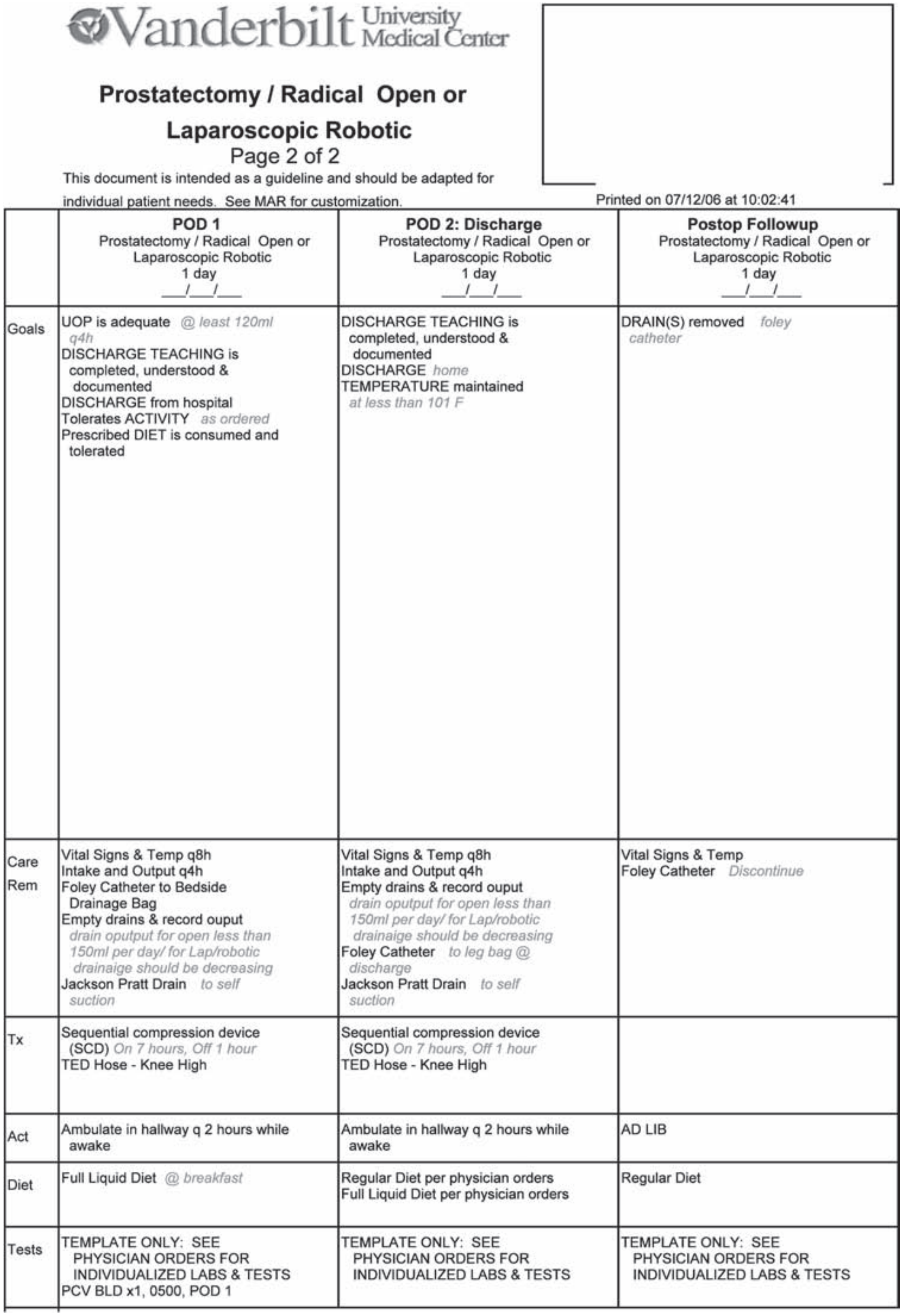
Figure 16.12 The Vanderbilt perioperative care pathway for radical prostatectomy.



Meds	TEMPLATE ONLY: SEE PHYSICIAN ORDERS FOR INDIVIDUALIZATION Bisacodyl: Dulcolax for open procedure *AM day before surgery* Magnesium Citrate Solution for Lap./Robotic procedure	TEMPLATE ONLY: SEE PHYSICIAN ORDERS FOR INDIVIDUALIZATION D5 1/2 NS + KCL 20 Meq/l *@ 150 mL per hour* Cefazolin INJ: Ancef x1, prior to surgery *1 Gram IV* Ketorolac Trometh INJ: Toradol *IV in PACU and IV q6h x 36h* Dolasetron INJ: Anzemet PRN *for nausea* Acetaminophen: Tylenol PRN *for temp greater than 101F* Morphine Injection PRN x3d *IV for breakthrough pain* Prochlorperazine Inj: compazine PRN *Give if nausea unrelieved by anzemet (dolasetron)* Enoxaparin INJ: Lovenox Subcutaneous daily *for open procedure only* Oxybutynin Chloride: Ditropan PRN *bladder spasms* BELLADONNA-OPIUM 16A Supp 3 Day PRN *bladder spasms- see physician orders* Laxative of Choice -See physician orders- Analgesic See physician orders *for oral analgesic* MED: Misc esomeprazole magnesium (nexium)
Cons	Case Manager Consult VPEC	
Tch	Tch: Physician instructs re procedure anticipated, risks & benefits, etc. Tch: Orientation to VUMC *Where family will wait, parking, etc.* Tch: Preop Processes *Where & when to arrive for surgery,etc.*	Tch: Postop *Unit routines, TC&DB care practices* Tch: When/How to Request Pain Medication
Disch Plan	CCP: Anticipated LOS and plan of care per pathway *Anticipated 1-2 day length of stay* CCP: Initiate Discharge Planning *Notify CM/ CNS of patients/families with special needs.* CCP: Misc *Coordinate physicial exam with PCP*	CCP: Admission History & Discharge Plan *Initiated*
Notes		

Signature	Init	Signature	Init	Signature	Init	Signature	Init

Figure 16.12, cont'd.



Vanderbilt University Medical Center

Prostatectomy / Radical Open or Laparoscopic Robotic

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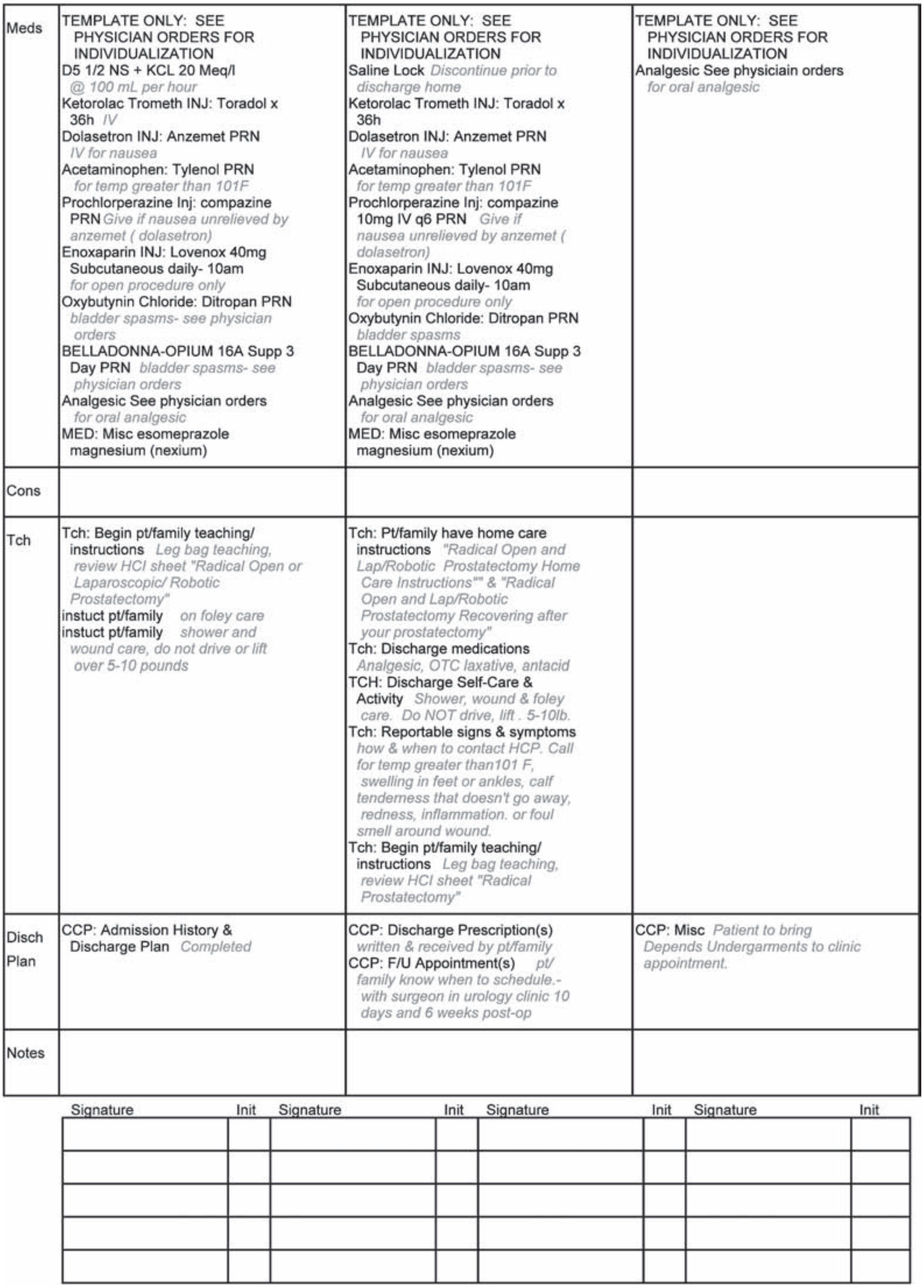
	POD 1 Prostatectomy / Radical Open or Laparoscopic Robotic 1 day __/__/__	**POD 2: Discharge** Prostatectomy / Radical Open or Laparoscopic Robotic 1 day __/__/__	**Postop Followup** Prostatectomy / Radical Open or Laparoscopic Robotic 1 day __/__/__
Goals	UOP is adequate *@ least 120ml q4h* DISCHARGE TEACHING is completed, understood & documented DISCHARGE from hospital Tolerates ACTIVITY *as ordered* Prescribed DIET is consumed and tolerated	DISCHARGE TEACHING is completed, understood & documented DISCHARGE *home* TEMPERATURE maintained *at less than 101 F*	DRAIN(S) removed *foley catheter*
Care Rem	Vital Signs & Temp q8h Intake and Output q4h Foley Catheter to Bedside Drainage Bag Empty drains & record ouput *drain oputput for open less than 150ml per day/ for Lap/robotic drainaige should be decreasing* Jackson Pratt Drain *to self suction*	Vital Signs & Temp q8h Intake and Output q4h Empty drains & record ouput *drain oputput for open less than 150ml per day/ for Lap/robotic drainaige should be decreasing* Foley Catheter *to leg bag @ discharge* Jackson Pratt Drain *to self suction*	Vital Signs & Temp Foley Catheter *Discontinue*
Tx	Sequential compression device (SCD) *On 7 hours, Off 1 hour* TED Hose - Knee High	Sequential compression device (SCD) *On 7 hours, Off 1 hour* TED Hose - Knee High	
Act	Ambulate in hallway q 2 hours while awake	Ambulate in hallway q 2 hours while awake	AD LIB
Diet	Full Liquid Diet *@ breakfast*	Regular Diet per physician orders Full Liquid Diet per physician orders	Regular Diet
Tests	TEMPLATE ONLY: SEE PHYSICIAN ORDERS FOR INDIVIDUALIZED LABS & TESTS PCV BLD x1, 0500, POD 1	TEMPLATE ONLY: SEE PHYSICIAN ORDERS FOR INDIVIDUALIZED LABS & TESTS	TEMPLATE ONLY: SEE PHYSICIAN ORDERS FOR INDIVIDUALIZED LABS & TESTS

Figure 16.12, cont'd.



Meds	TEMPLATE ONLY: SEE PHYSICIAN ORDERS FOR INDIVIDUALIZATION D5 1/2 NS + KCL 20 Meq/l *@ 100 mL per hour* Ketorolac Trometh INJ: Toradol x 36h *IV* Dolasetron INJ: Anzemet PRN *IV for nausea* Acetaminophen: Tylenol PRN *for temp greater than 101F* Prochlorperazine Inj: compazine PRN *Give if nausea unrelieved by anzemet (dolasetron)* Enoxaparin INJ: Lovenox 40mg Subcutaneous daily- 10am *for open procedure only* Oxybutynin Chloride: Ditropan PRN *bladder spasms- see physician orders* BELLADONNA-OPIUM 16A Supp 3 Day PRN *bladder spasms- see physician orders* Analgesic See physician orders *for oral analgesic* MED: Misc esomeprazole magnesium (nexium)	TEMPLATE ONLY: SEE PHYSICIAN ORDERS FOR INDIVIDUALIZATION Saline Lock *Discontinue prior to discharge home* Ketorolac Trometh INJ: Toradol x 36h Dolasetron INJ: Anzemet PRN *IV for nausea* Acetaminophen: Tylenol PRN *for temp greater than 101F* Prochlorperazine Inj: compazine 10mg IV q6 PRN *Give if nausea unrelieved by anzemet (dolasetron)* Enoxaparin INJ: Lovenox 40mg Subcutaneous daily- 10am *for open procedure only* Oxybutynin Chloride: Ditropan PRN *bladder spasms* BELLADONNA-OPIUM 16A Supp 3 Day PRN *bladder spasms- see physician orders* Analgesic See physician orders *for oral analgesic* MED: Misc esomeprazole magnesium (nexium)	TEMPLATE ONLY: SEE PHYSICIAN ORDERS FOR INDIVIDUALIZATION Analgesic See physiciain orders *for oral analgesic*
Cons			
Tch	Tch: Begin pt/family teaching/ instructions *Leg bag teaching, review HCI sheet "Radical Open or Laparoscopic/ Robotic Prostatectomy"* instuct pt/family *on foley care* instuct pt/family *shower and wound care, do not drive or lift over 5-10 pounds*	Tch: Pt/family have home care instructions *"Radical Open and Lap/Robotic Prostatectomy Home Care Instructions"" & "Radical Open and Lap/Robotic Prostatectomy Recovering after your prostatectomy"* Tch: Discharge medications *Analgesic, OTC laxative, antacid* TCH: Discharge Self-Care & Activity *Shower, wound & foley care. Do NOT drive, lift . 5-10lb.* Tch: Reportable signs & symptoms *how & when to contact HCP. Call for temp greater than101 F, swelling in feet or ankles, calf tenderness that doesn't go away, redness, inflammation. or foul smell around wound.* Tch: Begin pt/family teaching/ instructions *Leg bag teaching, review HCI sheet "Radical Prostatectomy"*	
Disch Plan	CCP: Admission History & Discharge Plan *Completed*	CCP: Discharge Prescription(s) *written & received by pt/family* CCP: F/U Appointment(s) *pt/ family know when to schedule.- with surgeon in urology clinic 10 days and 6 weeks post-op*	CCP: Misc *Patient to bring Depends Undergarments to clinic appointment.*
Notes			

Signature	Init	Signature	Init	Signature	Init	Signature	Init

Figure 16.12, cont'd.

incision for RRP is usually easily managed. Although epidural catheters, intrathecal narcotic injection, or patient-controlled analgesia using intravenous narcotics are commonly employed, our pathway uses ketorolac administered immediately postoperatively and continued for 24 hours. Oral narcotic supplementation is allowed as required.

We have observed no difference in postoperative narcotic use in patients undergoing RRP vs RALP.[9] Furthermore, patient-reported pain scores are similar at multiple time points up to 2 weeks postoperatively. The primary reason for the lack of difference is the low pain scores in both groups with a median of less than 3 on a scale of 10 at all time points. These findings indicate that RALP can be performed with minimal postoperative patient pain but that the same statement applies to RRP.

Length of stay

Over the last decade, the length of hospital stay for patients undergoing radical prostatectomy has declined dramatically. Initially, we constructed a pathway which targeted postoperative day 3 for discharge but subsequently reported routine discharge on postoperative day 2. For the last several years, the pathway uses postoperative day 1 for the targeted discharge date for either RRP or RALP. Patients in the RALP group achieve this goal a little more commonly (94% vs 86%).[10]

Prolonged ileus is the most common medical reason for failure to meet the discharge target of postoperative day 1. Unscheduled clinic or emergency room visit after discharge occurs in 5% and 6% of the RRP and RALP groups, figures which are no different than those reported when the average length of stay is longer. Thus, the safety of an early discharge program is well established.

An important determinant of length of stay is patient preparation.[11] Patients must plan for discharge to arrange both transportation and a supportive environment at home. Liberal use of a visiting nurse program can also facilitate discharge. If there is excessive drainage, patients are discharged with their closed suction drain in place and then return for drain removal pending telephone follow-up and recording of drain output.

Return to activities

A more rapid recovery and return to full activities is often touted as an advantage of RALP. However, there are no good prospective studies to validate this premise. The postoperative instructions we give patients are identical regardless of surgical approach. The Foley catheter is left indwelling for a week and patients are allowed to drive a car after 10 days. Even though the surgical incisions for placement of the laparoscopy ports are small, port site hernia can occur. This is especially true at the umbilical port site, which is enlarged for extraction of the surgical specimen. Therefore, patients are advised against strenuous activity for 1 month after surgery. We are evaluating patient reported quality of life postoperatively to see if there is a discernible difference between the two surgical approaches.

Incontinence

Most men place fear of incontinence as their Number 1 concern with radical prostatectomy. Fortunately, severe incontinence is unusual; however, at least some leakage occurs in at least 10% of men and in higher proportions in many studies based upon public databases.[12,13] The technical steps to avoid incontinence have been described in multiple publications but there is still a great deal of uncertainty about why some patients develop problems.[14,15] Nonetheless, preservation of the sphincter muscle and the tissues of the genitourinary diaphragm is key toward avoiding incontinence.

Because of the excellent visualization of the prostatic apex and the minimal disturbance of the genitourinary diaphragm with RALP, it has been proposed that the rate at which continence returns is improved and that fewer patients have long-term difficulties. On the other hand, this premise is challenged by highly experienced open surgeons who claim comparable results.

In our prospective single surgeon series, we have been unable to demonstrate statistically significant differences in return of urinary control at 3 months, 6 months or 12 months after surgery whether the patient has an RALP or RRP.[16] There is a small trend in favor of the RALP group but not enough for statistical significance. Anchoring the urethra and bladder neck to the severed puboprostatic ligaments and pubis is used by both open and laparoscopic surgeons in an effort to improve results with continence. This and other measures need continued exploration to try to lower further the risk of incontinence after radical prostatectomy.

Erectile dysfunction

Although not a priority issue for all men undergoing radical prostatectomy, erectile dysfunction looms as the largest statistical risk a man undergoing radical prostatectomy faces. Results are dependent upon patient age, preoperative erectile status, and surgeon experience. What remains a question is whether the results also depend upon surgical approach.[17]

There are several potential reasons why RALP could provide superior outcomes for erectile function. First of all, the superb visualization allows precise dissection of the neurovascular bundle. The antegrade approach may lessen traction injury, especially at the prostatic apex. The tamponade effect of the pneumoperitoneum compresses venous bleeding and further improves visualization.

An important surgical judgment which may affect outcome with nerve sparing is how much hemostasis has to be achieved. Certainly it is important to keep the operative field clean for visualization. However, there is always some degree of oozing along the neurovascular bundles. Complete hemostasis could be obtained, but this would risk damage to the neurovascular bundle. Once the anastomosis is complete, this bleeding usually stops whether open or laparoscopic surgery is being performed. Thus, it is important to avoid overzealous hemostasis. Some techniques for RALP use either monopolar or bipolar cautery to release the neurovascular bundle. RALP is, then, sometimes criticized by open surgeons who perceive a necessity for electrocautery along the neurovascular bundle with RALP. However, the technique we use and techniques described by others avoid all thermal injury along the neurovascular bundle.

Again, comparisons of results between series of RALP and those of highly experienced open surgeons are difficult because of variance in collection and reporting of data. Good results have been achieved with both surgical approaches and there is ongoing debate about whether one technique is superior to the other.[14,15,18] However, there is emerging information to suggest that, with experience, surgeons can achieve preservation of potency with RALP at a rate somewhat higher than that for RRP. In our own experience, we have not been able to demonstrate a statistically significant improvement in return of potency with RALP, although there is a trend in that direction.

Positive margins

Perhaps the most contentious issue with regard to RALP has been the status of tumor margins. Virtually all studies have shown a high positive margin rate early in a surgeon's experience with RALP.[19,20] Parenthetically, there are parallel studies which show a higher positive margin rate for surgeons inexperienced with RRP. Nonetheless, this becomes an issue for a surgeon considering a transition from open radical prostatectomy to RALP.

There is no inherent reason why, given comparable experience, there will be a substantial difference in margin status between different surgical approaches.[21,22] The most important factor influencing margins is patient selection. However, method and detail of histological analysis and reporting are also extremely important. Because of differences in these measures, comparison from one series to another is fraught with error.[23]

Our prospective comparative series at the Vanderbilt University Medical Center has confirmed and underscored the reported experience from other centers. It is important to point out that our definition of a positive margin does not depend upon subsequent or additional biopsies. Furthermore, an incision into a tumor-bearing portion of the prostate, even if corrected, is still considered a positive margin. With experience, we have observed a progressive decrease in our positive margin rate. Importantly, in our last 300 patients undergoing RALP, the T2 positive margin rate is lower than that for RRP, with the difference being statistically significant ($p < 0.05$). These data imply that the loss of tactile feedback with RALP is not an important factor in achieving negative surgical margins. In addition, if the surgeon wants to perform immediate examination of the surgical specimen, the prostate can be extracted shortly after removal and inspected, just as may occur with open surgery.

Training requirements

Performance of RALP requires acquisition of a new skill set for many surgeons. As discussed above, lack of experience with the technique can affect some important patient outcome measures. Although this observation is not unique to RALP, it does emphasize the importance for surgeons of undergoing proper training and gaining appropriate experience before widely adopting RALP.

The importance of the entire operative team cannot be overemphasized. Many reports have used duration of surgery as the primary method to assess the learning curve. The duration of surgery is, to be sure, partly dependent upon the console surgeon. However, an operative team experienced with set up and docking of the robot, instrument changes, and surgical assistance greatly facilitates performance of the operation.

Although the anatomical considerations are identical to RRP, the magnified view and antegrade dissection may be somewhat unfamiliar to open surgeons. Observation of surgical procedures and videotapes can be useful measures to develop familiarity with the anatomy.

The learning curve is frequently discussed but poorly defined. It is a self-declared point at which the surgeon can provide outcomes comparable to alternative approaches in his hands. Thus, the target efficiency depends upon the expectation and experience of the surgeon. Reports that 20–25 cases are required to overcome the learning curve are probably gross underestimates.

Training of residents and fellows is seemingly less an issue than for established practitioners. The progressive, graduated experience during residency facilitates learning of the technique. Furthermore, residents have the opportunity to observe and assist in multiple procedures before assuming increasing responsibility at the console. Practitioners may have the same opportunity if there are surgeons experienced with RALP in their hospital.

CONCLUSIONS

Robot-assisted laparoscopic prostatectomy in only a few years has assumed an important role in the surgical management of carcinoma of the prostate. Whereas some of the interest in the procedure is fueled by marketing and promotional efforts, there are demonstrated patient advantages. Once facility with the procedure is obtained, even a highly experienced open surgeon can achieve results that match or exceed outcomes with radical retropubic prostatectomy. As with open surgery, adherence to sound surgical and oncological principles is key in achieving the desired outcomes.

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CHAPTER 17

Radical prostatectomy – making the transition from open to robotic surgery: the London experience

Roger S Kirby, Miles A Goldstraw, Prokar Dasgupta, Chris Anderson, Krishna Patil, Peter Amoroso, and Jim Peabody

INTRODUCTION

Over the past two decades, open nerve-sparing radical retropubic prostatectomy (RRP) has become widely established worldwide as a safe and effective treatment for localized prostate cancer. Recent data from Scandinavia have confirmed that, compared with watchful waiting, radical prostatectomy (RP) reduces the risk of developing metastases by around 50% and improves the chances of prostate cancer specific and overall survival.[1] Not withstanding this, open RRP is still a fairly formidable operation to perform, and even more so to undergo. The lower abdominal incision is associated with significant postoperative discomfort, many patients find the period of up to 3 weeks postoperative catheterization tiresome, and convalescence is often slow.

Although in expert hands cancer clearance rates (i.e. negative surgical margins and no evidence of biochemical failure) are high, and persistent urinary incontinence is unusual, many patients suffer permanent erectile dysfunction that does not always respond to phosphodiesterase type 5 inhibitors.

The first serious surgical challenge to open RRP came from the laparoscopists in France who discovered that both intraperitoneal[2,3] and extraperitoneal[4] laparoscopic RRP were feasible. Advantages over open RRP in terms of reduced blood loss[5] and diminished postoperative pain[6] soon became apparent, and patients were also able to return to normal activities more rapidly. The major problem with laparoscopic RRP relates to the difficulty in learning the procedure. The counterintuitive movements required to control the laparoscopic instruments, especially when dissecting and suturing deep in the pelvis, take many months to master. This makes the learning curve long and exposes patients to risk of complications while the necessary experience is gained. By contrast, robot-assisted RRP is somewhat easier to master, because of the more intuitive way in which the instruments are controlled, and the three-dimensional vision with up to 10 times magnification.

In this chapter we describe the way in which our group accomplished the transition from open to robotic RRP. We do not pretend that the journey has been an easy one, but we have recently completed our 200th robotic prostatectomy without any major complications. Although we consider this an important milestone, we do not pretend to have mastered this technique. Certainly others are in a better position to lay claim to this, with Dr Mani Menon at the Vattikuti Institute, Henry Ford System, Detroit, USA having reported results from 1100 robotic RRP cases.[7] The learning curve for robotic RRP may differ significantly according to a number of surgeon-related factors. Herrell et al[8] reported that >150 cases needed to be performed before all outcome variables reached parity with the open technique. Furthermore, >250 cases needed to be performed before confidence levels of the operating surgeon were similar to the open technique. These figures have important implications for any group intending to set up a robotic prostatectomy program. The median number of radical prostatectomies performed by urologists in the USA is only seven cases per year; clearly, at this rate, many will never overcome the learning curve.[8]

MAKING THE TRANSITION

For those considering making the transition, the first step, of course, is the acquisition of a da Vinci robot; this is a considerable investment for any institution.[9] Additional funds will have to be allocated for the service contract and the ongoing costs of robotic instruments, such as scissors, forceps, and the diathermy hook. The robotic cart weighs something in the order of 2 tons and the operating department floor has to be sufficiently robust to withstand this weight. The console is light but there has to be sufficient space for both of these bulky pieces of equipment (Figures 17.1a and 17.1b).

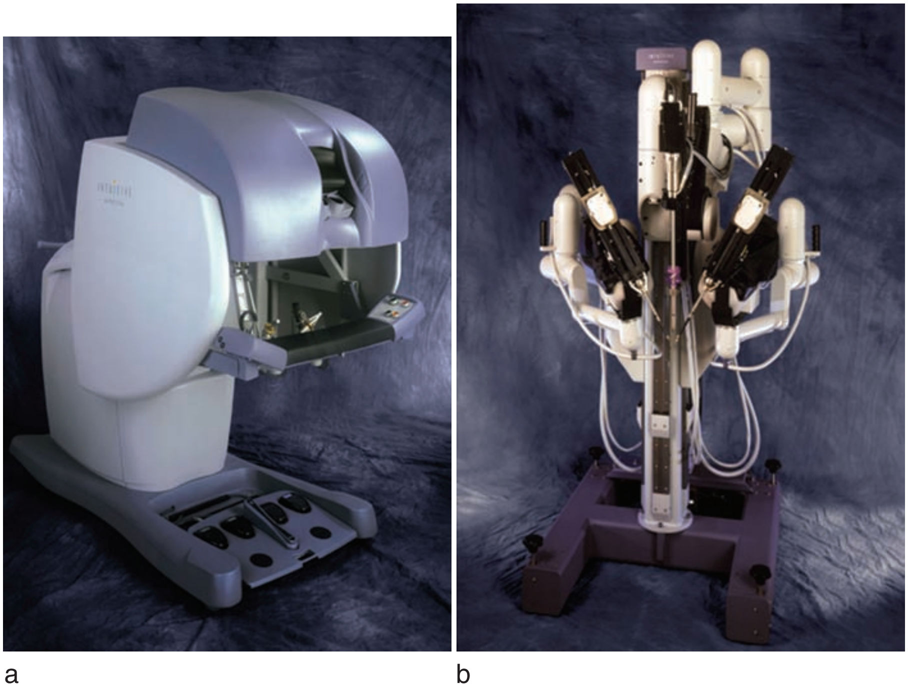

Figure 17.1 (a) The da Vinci console. (b) The da Vinci surgical cart.

Once the robot is installed, structured training of the nursing and medical team is required. Careful selection of surgical team members is advisable: we combined a surgeon who was very experienced in open RRPs (R.S.K. – more than 1200 cases performed) with an experienced laparoscopic prostatectomist (C.J.A.) and the UK's first robotic urologist (P.D.) who had been using the da Vinci robot to perform radical cystectomy, colposuspension, live donor nephrectomy, and pyeloplasty. We started with so-called wet lab training in New York, where we operated robotically on an anesthetized pig and also observed an experienced team undertaking robotic RRP from start to finish. We were then fortunate to have Dr Jim Peabody, who has worked closely with Dr Mani Menon to develop the procedure, come across to the UK to mentor the group. It has to be said that the greatest obstacle to this was the rules and regulations imposed by the UK General Medical Council (GMC), who contrived to make the process of temporary registration as labyrinthine as possible. Eventually, the bureaucrats were satisfied and Jim joined us to guide us through our first six cases. These were accomplished over 5 consecutive days, informed consent having been achieved from patients who were aware that this was a new undertaking for us. Fortunately no complications were encountered, in spite of the sometimes prolonged (up to 6 hours) duration of the procedure during this early stage of our experience.

Six cases safely completed, but were we ready to 'go it alone'? Categorically no; for us, mastering the numerous steps required to perform robot-assisted RRP needed more mentoring support, so we persuaded Jim Peabody to return for a further 6 cases. We also managed to inveigle Dr Ashutosh Tewari from Cornell, New York, who had been in Detroit with Dr Mani Menon while the robotic technique was being developed, to come across and help us with a further two cases. Thus, before we went solo we were mentored and supported through a total of 14 robotic RRPs. Even then, the next few cases were a little nerve wracking, but as the confidence and skill of the team grew, the operating time diminished and the benefits of the procedure from the patient's viewpoint became increasingly apparent.

SURGICAL TIPS FOR THE SAFE PERFORMANCE OF ROBOTIC RRP

The goal of RRP is identical to that of open surgery: complete removal of the prostate and seminal vesicles (hopefully with clear margins and a good functional outcome). The role of pelvic lymphadenopathy is controversial and while it is not difficult to perform via the robotic technique we have reserved this for higher-grade cancers or those with high prostate-specific antigens (PSAs >15 ng/ml). Both extraperitoneal[10] and transperitoneal approaches[11] are feasible; however, we adopted the technique of Dr Mani Menon, preferring to undertake a transperitoneal approach with antegrade dissection.

Selection criteria are virtually the same for RRP as with open surgery. Whereas obesity is not a particular problem for the operating surgeon (extra-long laparoscopic instruments may be needed), it does appear these patients do worse following this surgery. Ahlering et al noted that baseline sexual and urinary function were significantly worse (vs non-obese comparison) and that there was a strong trend towards delayed recovery time.[12] Obesity may also be a problem for the anesthetist, with Trendelenburg tilt and high intra-abdominal pressure making ventilation difficult. The authors have performed a number of cases with large prostates (>100 cc); however, we recommend leaving these until greater confidence is gained. RP can be an extremely difficult procedure following mesh repair of hernia, but with transperitoneal RRP this has not been a major problem. Any adhesions have to be carefully dissected in the initial phase of the operation, but once complete you are able to proceed as planned. During the first 100 cases, we have identified and treated laparoscopically a number of undiagnosed inguinal hernias. This procedure takes a matter of a few minutes and involves the insertion of a Prolene mesh, which is maneuvered around the cord and stapled into position, which would not be possible with the open technique.

After the patient is anesthetized and correctly positioned with all pressure points protected, the abdominal skin is prepared and a urethral catheter passed. Establishing access to the prostate within the pelvis via a transperitoneal route requires safe and careful placement of 6 laparoscopic ports (2 robotic, 2 × 10 mm, 2 × 5 mm). The first key maneuver is the safe establishment of the pneumoperitoneum, which is accomplished though a small vertical incision adjacent to the umbilicus. The fat is dissected down to the level of the rectus sheath, which is elevated using two strong sutures. A 2 mm incision in the sheath is made and a Veress needle cautiously introduced into the peritoneal cavity while an assistant pulls upward on two sutures that have been placed in the rectus sheath. Correct placement of the Veress needle is checked by injection of saline before CO_2 is connected. As the pneumoperitoneum is established, careful checks should be kept on the pressure, which should not rise above a few mmHg until several liters are infused, providing that the needle is correctly sited. Incorrect placement of the Veress needle is usually in the extraperitoneal space or within the omentum, but rarely a puncture of the small bowel or other intra-abdominal viscus may occur. Provided this is recognized early, little harm will ensue. If difficulties are encountered with the insertion of the Veress needle, an open insertion of the midline camera port trocar should be performed. Once the camera port is correctly in place, the other 5 ports can be created under direct vision using a 30 degree up lens. Correct port placement is critical, and the optimum position of each port is shown in Figure 17.2.[13] It is essential that any preexisting adhesions, from for example a previous appendicectomy scar, be divided laparoscopically, so that safe and secure port placement can be achieved. Care must be taken during this adhesiolysis, as underlying bowel is often extremely close without necessarily being seen; unidentified diathermy injury to bowel has been reported requiring delayed laparotomy.[14] In two of our first 100 cases, intra-abdominal adhesions were so extensive that a decision was made after insertion of the camera port, to place no further ports and proceed instead with an open extraperitoneal procedure.

The next move is to dock the robot. The machine is advanced between the patient's legs and the camera port connected, ensuring that the robotic cart is central and that the camera arm is correctly positioned. A 30 degree up telescope is utilized for the first part of the procedure. The second, third, and optional fourth robotic arms are then connected and each port inspected in turn to ensure correct positioning and to exclude significant intraperitoneal bleeding. The instruments are then introduced under direct vision and the surgeon at the console then takes over their control.

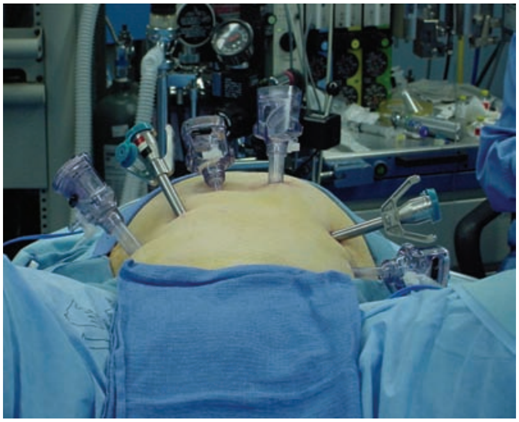

Figure 17.2 Ports in place prior to docking of the da Vinci robot.

The bladder is mobilized fully at the time of takedown of the peritoneum. Adhesions to the bladder should be released and the ‘inverted-U’ peritoneal incision should be taken down to the level of the vas on each side. The vasa can be divided laterally at the point they cross the medial umbilical ligament to achieve more mobility of the bladder and to allow for easier access to lymph node packets. This additional mobility can allow for easier movement of the bladder to the urethra during anastomosis. An assistant or the fourth arm can grasp the bladder anteriorly to hold down the bladder as well.

In very overweight patients with a large amount of perivesical fat, the bladder should not be taken down too high on the abdominal wall, as this leaves extra weight on the bladder, which can serve to distract the bladder cranially away from the anastomosis later.

Once the prostate is exposed, scrupulous attention is paid to the removal of the fat that lies on its anterior surface using the 0 degree telescope. This must be accomplished with care, as bleeding may occur from the fragile superficial veins that lie within it, usually in the midline. These can be diathermied with the bipolar forceps. The next move is to divide the lateral pelvic fascia on each side to mobilize the prostate. This plane is usually relatively bloodless, but care does need to be taken as the prostate–urethral junction is approached to avoid injury and bleeding from the dorsal venous complex. The muscle of the pelvic floor is gently teased away from the urethra, so that the suture to secure the dorsal venous complex can be placed under direct vision. The puboperinealis muscle covers the urethra and is the most anteromedial component of the levator ani; this appears to have a special role in the urinary continence mechanism.[15] Inferiorly, the incisions are deepened until a characteristic triangle of fat is identified that marks the vesicoprostatic junction. The instruments are then changed to two needle drivers and a suture placed through the groove between the dorsal venous complex and the urethra from right to left and then brought back from left to right immediately beneath the puboprostatic ligaments and then tied securely on the right-hand side of the urethra. The puboprostatic ligaments fix the prostate to the pubis, maintain support for the striated sphincter,[16] and help prevent hypermobility of the penis.[17] Certainly, a number of groups feel that puboprostatic preservation is important in helping gain early continence.[18,19]

The next move is to dissect the prostate away from the bladder neck using the 30 degree down telescope. It is important that this incision is made precisely in the correct location to avoid an inadvertent incision into the anterior prostate, which can cause confusion and additional bleeding. Pinching the prostate bilaterally to define the vesicoprostatic junction can be helpful, as can be traction applied to the catheter. The relatively thin anterior bladder neck is divided in the midline down to the catheter, which is identified and the balloon deflated. The catheter is then pulled through and held up by the second assistant or the fourth arm to apply anterior traction to the prostate. This maneuver facilitates the incision through the posterior bladder neck, which must be beneath any median lobe but well away from the usually easily visualized ureteric orifices. Once the posterior bladder neck is divided, the incision is deepened through Denonvilliers’ fascia; at this point, care has to be taken to avoid either buttonholing of the bladder neck or inadvertent incision into the prostate itself. Provided the correct plane is located, the vasa and seminal vesicles come into view quite quickly. The right vas is dissected free and divided and then the first assistant is requested to grasp and lift the proximal end of the vas. This facilitates the dissection of the right seminal vesicle, which is elevated progressively as the vesicular arteries are secured and divided by diathermy. The procedure is then repeated for the left vas and seminal vesicle. Once both seminal vesicles are free, the second assistant or fourth arm is used to elevate the prostate by lifting up on them and the proximal stumps of the divided vasa. A 'window' is then apparent just behind the posterior prostate and anterior to the rectum.[20] An incision here soon exposes the prerectal fat and the rectum can be pushed gently backwards as the posterior prostatic capsule comes into view. Extending the dissection right and left at this point can facilitate the subsequent dissection of the neurovascular bundles. Sometimes a switch back to the 0 degree telescope can be helpful. Once the apex is reached, attention is paid to securing each prostatic pedicle, which is done using so-called Weck clips and the robotic scissors.

The dissecting scissors are then used to dissect the neurovascular bundles on each side. If a nodule is palpable, a wide excision may be indicated on the side affected in an attempt to achieve a negative surgical margin. Once this maneuver has been accomplished, the prostate should be free, apart from its connection to the urethra and ligated dorsal venous complex. These structures are then divided sharply by scissors to avoid diathermy injury to the distal urethral stump. Bleeding from the dorsal venous complex can usually be dealt with by bipolar diathermy and occasionally a suture. The prostate is then bagged and placed in the right iliac fossa.

As in open surgery, the anastomosis can be the most technically challenging part of the procedure; however, the superb vision and 10 times magnification facilitate this step considerably. Problems of suture pull-through at the bladder neck can be diminished by proper attention to the posterior bladder neck thickness at the time of division of the bladder off the posterior urethra – don't thin it out too much. At times, with a median lobe, the residual posterior bladder neck can be quite thin. In this case, a portion of the thinner tissue could be excised or, preferably, a deeper more secure bite into the bladder can be taken.

Bleeding from the dorsal vein complex and prostatic pedicles should be controlled as necessary to allow for clear vision before division of the urethra. This allows for better visualization and facilitates creation of a good urethral stump. It also allows for improved ability to see the urethra during suturing and make the urethra more prominent. Perineal pressure can help to demonstrate bleeding points at the dorsal vein, which can facilitate precise suture ligature.

For bladder neck tapering, it is important to have a rough concordance (not more than 2–3:1) between the bladder neck and urethra; however, a larger bladder neck is easier to anastomose than a smaller one. Sutures can be placed laterally at the 3 o'clock and 9 o'clock positions. We typically use interrupted 3-0 Vicryl (polyglactin) on an RB-1 needle. Care must be taken to avoid the ureteric orifices, which can usually be visualized well. Indigo carmine or methylene blue could be injected intravenously for their easier identification but we have not had to do this. If the bladder neck is too small, 1–2 tapering sutures could be removed or if no tapering was done an incision could be made at the 12 o'clock position (anterior) on the bladder to improve visualization of the posterior (trigonal) bladder neck. Sometimes we perform an anterior tapering; i.e. we complete the anastomosis leaving a gap anteriorly, which is closed separately in a 'tennis racket' fashion.

The pneumoperitoneum causes the urethra to be extruded out of the pelvis, which can make it difficult to accurately place the initial sutures. Perineal pressure is used routinely to evert the urethra at the beginning of the anastomosis. It is used until the bladder is snugged down to the urethra, creating the posterior plate.

Use of a urethral catheter throughout anastomosis allows for accurate visualization of the urethra. It prevents 'backwalling' of the urethra. Prior to each suture being placed through the urethra, the tip of the catheter is passed forward by the assistant to allow visualization of the urethra and a minimal degree of urethral eversion. The catheter must be well lubricated. The catheter should be withdrawn a few centimeters by the assistant prior to the bladder bite being taken to assure that the catheter is not pierced by the needle. The catheter should be changed after completion of the anastomosis.

Sugundh Shetty from William Beaumont Hospital, Detroit described a technique to us whereby a long Prolene (polypropylene) suture is passed through the bladder neck in the midline. A Foley catheter is then placed through the urethra into the pelvis. The ends of the Prolene suture are then passed through the eye of the catheter, and the catheter is withdrawn through the urethra, pulling the ends of the Prolene suture out through the meatus. Traction on this suture will approximate the bladder neck to the urethra, facilitating the anastomosis.

We use the 0 degree lens for the anastomosis and the ‘MVAC’ suture exclusively: this suture was the result of a series of communications between Dr **M**enon,[18] Professor **V**an Velthoven,[21] Dr **A**hlering, and Dr **C**layman. A double-armed suture is created by tying two 3-0 Monocryl (poliglecaprone) sutures together with a ‘ten-throw’ knot, which creates a pledget. The arms are 6–7 inches long. One arm may be dyed and the other undyed to allow for easier identification of the right and left sides. An RB-1 needle is used on each end. The dyed end is used first. At times, the bladder neck can be difficult to identify. It these circumstances we will use the needle in the right hand to try to engage the posterior bladder neck and elevate it into view. If this is not successful, the lens could be switched to 30 degrees down to find the bladder neck. The assistant can also use the suction to press the anterior portion of the bladder down and cephalad to further expose the urethra. Some groups have suggested placing a suture on the posterior bladder neck, at the time of division of the bladder from the prostate, to facilitate later identification, but we have never found this necessary.

The dyed end is run from the 4 o’clock position in a clockwise fashion to the 11 o’clock position. An outside-in bite is taken at the 4 o’clock position on the bladder neck, just lateral to the right ureteral orifice. This suture must be pulled through until the knot is secure and tight against the bladder muscle. The next bite is taken inside-out in the urethra at the corresponding 4 o’clock position using the perineal pressure and catheter as noted above. The next bite is taken outside-in on the bladder neck, again in the midline. The next bite is inside-out on the urethra in the midline. With these first 2 urethral bites, an effort is made to include a few millimeters of tissue posterior to the urethra to provide a more secure bite. The next pass of the suture is outside-in on the bladder at the level of the left ureteral orifice. With these 5 bites placed (3 bladder and 2 urethral), the bladder can be gently pulled down to the urethra by using the left hand to pull on the dyed suture and the right-hand needle driver to push the bladder neck down. The instrument can be placed behind the trigone to push the bladder forward.

Once the posterior plate is securely together, the assistant on the right side will hold traction on the suture while the console surgeon will use both needle drivers to place the next suture (inside-out on the urethra). Some surgeons will perform a single-, double-, or even a triple-locking suture at this point. One or two additional bites are taken inside-out on the urethra and outside-in on the bladder. After each bladder bite is secured, we have the right-sided assistant hold tension on the suture. As an alternative, the console surgeon can hold the tension on the suture, but this requires a higher degree of skill as the needle must be manipulated with only one instrument. This is not recommended for the novice robotic surgeon. The mucosa should be visualized and taken with each bite on each side. The suture is then ‘turned around’ on the bladder by placing a suture outside-in and then inside-out on the bladder. This serves to both make up some of the difference in size between the bladder and urethra and to allow for easier suturing on the left-side anterior urethra; additional bites are taken, outside-in on the urethra and inside-out on the bladder. Suturing continues for 1 or 2 more bites until the 11 o'clock position is reached. The suture can then be held by the left-side assistant, the fourth arm, or secured to the side wall or bladder.

The right side of the anastomosis is then completed by placing the first pass of the undyed suture outside-in on the urethra, the next bite being inside-out on the bladder. These initial bites are sometimes easier to perform with a right-handed backhand approach. Additional bites are taken in sequence until the anastomosis is complete.

The anastomosis should be inspected to be certain that all sutures are pulled down tight. Any gaps should be tightened. Then the suture is tied. We generally cut the needle off the dyed suture because this suture end is more easily visualized than the undyed one. We use a single-throw first knot and make an effort to gently pull the sutures horizontally, watching for an indentation in the bladder muscle to indicate that the suture is tight. Six to seven throws are taken and the suture ends are trimmed.

Fluid along the sides of the bladder and anastomosis is suctioned out. A new catheter is advanced into the bladder up to the hub. The balloon is not yet inflated. The bladder is filled with 120–180 cc of saline to check for leaks. If none are found, the catheter is inflated and the anastomosis is complete.

If a leak is found, the new catheter is removed and the old one replaced. This is to prevent damage to the new catheter during the attempted repair of the leak. We identify the leak with the bladder partially filled. A 3-0 Vicryl on an RB-1 needle is used to close the leak, usually with a figure-of-eight suture. After each pass of the needle, the catheter should be advanced into the bladder to assure that the needle has not 'backwalled' the urethra or bladder, narrowing the anastomosis. A posterior leak is very difficult to close. A large leak is best treated by prolonged catheterization or takedown and reconstruction of the anastomosis. A leaking anastomosis can be treated by a period of light tension on the Foley catheter.

Before closure, a suction drain is placed under vision on the anterior bladder wall. Some surgeons suture the peritoneum back in place (puboperineoplasty) but this is usually unnecessary. The robot is undocked and the prostate removed through an enlarged paraumbilical incision. The wounds are then closed carefully, with particular attention to the larger port entry sites to minimize the risk of hernia formation and subcuticular sutures used to close the skin.

POSTOPERATIVE CONSIDERATIONS

Postoperatively, early mobilization is encouraged and the duration of hospital stay is a matter of 2–3 days only. Catheter removal can be accomplished within a few days but the risk of recatheterization is increased. We usually leave the catheter in place for 1 week, check hemoglobin, and carry out a urine culture. We recommend routine performance of a cystogram at the beginning of one's experience, and then as needed for more difficult anastomoses.

If a catheter falls out in the recovery room or shortly after surgery, we advise using a coude tip catheter with some rectal pressure to guide the catheter into the bladder. We obtain a cystogram to confirm correct catheter placement. It is extremely unusual to have complete disruption of an anastomosis, and this usually happens in the face of a large pelvic hematoma distracting the bladder from the urethra. In this situation it is feasible to laparoscopically re-explore the pelvis and re-do the anastomosis. This should be done as soon as possible after the problem is recognized – within a few days of the original operation. The tissues are often edematous and friable, and satisfactory completion of the anastomosis can be very difficult.

FUNCTIONAL OUTCOMES

Outcomes following robotic radical prostatectomy are controversial. Incontinence and erectile dysfunction are the complications with greatest effect on quality of life over the long-term. Surgical technique is undoubtedly a contributing factor to the stress incontinence seen after radical prostatectomy. Theoretically, the excellent vision provided by the laparoscopic camera, together with the minimal bleeding, allows precise dissection and limits trauma to the periurethral striated sphincter. This opens the door for the potential for early return of continence with RRP. Whereas results from RRP certainly show very low levels of incontinence,[18,22] none of the currently published studies show a definitive advantage over the open technique.

Since Binder and Kramer performed the first RRP,[23] it has been a continuously evolving technique, with continual refinements to the technique being made. Ong et al used a canine model to study the effects of thermal energy on the cavernous nerve function and their research supported strict avoidance of thermal energy around the neurovascular bundle.[24] Ahlering et al performed a prospective analysis of 59 potent men (SHIM scores 22–25), looking at short-term potency rates in men undergoing cautery-free robotic prostatectomy, and compared them with a closely matched control group undergoing standard bipolar diathermy dissection. Results showed a fivefold improvement (43% vs 8.3%) in 3-month potency with cautery-free prostatectomy compared with the standard bipolar dissection.[25] Chien et al showed broadly similar potency results of 47% at 3 months using a clipless antegrade nerve preservation approach.[26] Potency rates increased to 69% by 12 months and further long-term improvements may be expected. This study compares favorably with the outcomes for a series on open radical retropubic prostatectomy using the same validated questionnaire[27] (reporting 36.7 and 50%, 3- and 12-month intervals).

Menon et al have further refined the anatomical nerve-sparing robotic prostatectomy and reported that preservation of the prostatic fascia (the so-called veil of Aphrodite) is important for the maintenance of erectile function.[11] It is proposed that accessory neural channels exist in this lateral prostatic facia that may supply innervation to the penis. A recent report by this group has shown impressive results: prospective analysis of 76 potent men undergoing RRP with either standard robotic nerve-sparing prostatectomy (control) or the prostatic fascia-sparing technique (treatment) was performed. Patients with normal erectile function, low-risk disease (PSA < 10 ng/ml, stage T1c, Gleason score ≤6) were offered the prostatic fascia preservation technique (*n* = 46), although 8 patients were included in this group who did not fit this criteria exactly. Results at 12-month follow-up showed that 51% of treatment patients achieved normal erections compared with 17% of control patients[28] without medication. This percentage increased to 86% and 26%, respectively, with the use of a phosphodiesterase type 5 inhibitor and when the survey included all men able to achieve erection strong enough for intercourse. The figure reached 97% in the treatment group.

CONCLUSION

Although robotic radical prostatectomy is a relatively recent invention, it has already become a serious alternative to open prostatectomy. In the USA, there were already over 350 robotic systems performing over 35 000 procedures in 2006.[29] It is important not to be influenced too greatly by marketing claims, but there appear to be several benefits. Whereas laparoscopic radical prostatectomy results in reduced pain, low blood loss, and rapid patient recovery, it is an incredibly difficult operation to learn and one that has counterintuitive movements with no ergonomic comfort. In contrast, robotic RRP has all of the advantages of minimally invasive surgery and also has the benefits of 10× magnification, tremor reduction, ergonomic design, and intuitive movements (7 degrees of freedom). Theoretically, this may give improvements over traditional laparoscopy. Furthermore, any procedure that minimizes trauma to the periprostatic tissue has the potential to result in improved functional outcomes. This is suggested by recent data showing an improvement in erectile function with robotic RRP compared with the open approach.[28,30] Clearly, data from such a small number of patients need to be treated with caution, and outcome figures from specialist centers may not always be achievable elsewhere. However, robotic RRP is a continuously evolving technique, and outcome figures may be expected to continue to improve.[31] In comparison, open surgery has had two decades of improvements and may have reached a plateau in its development. Perhaps this is the key point that remains to be addressed and it will be crucial in deciding whether or not to make the transition. The other important factor is the health economics of robotic surgery: cost reduction can be anticipated in the future. However, it is possible that robotic RRP could become the new 'gold standard' treatment for clinically localized prostate cancer.

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CHAPTER 18

Radical prostatectomy: Making the transition from laparoscopic to robotic surgery: the University of Rochester experience

Jean V Joseph and Hitendra Patel

Open radical prostatectomy has been the gold standard in the surgical management of prostate cancer. Over the last decade laparoscopic radical prostatectomy (LRP) and, more recently, robotic radical prostatectomy have emerged as viable options challenging the open approach. In this chapter we evaluate these two newer modalities in an effort to better determine their role in the evolving field of prostate cancer management. The technical aspects of these procedures are covered elsewhere in this book and are beyond the scope of this chapter.

The application of laparoscopic technology to remove a cancerous prostate debuted in 1992 when Schuessler et al from Washington University reported the first case.[1] However, it took 5 years for them to report an additional 5 cases in the literature.[2] Due to the difficulty associated with the procedure, the authors concluded that the procedure was too long and offered no advantages over the open approach. LRP remained experimental until Guillonneau and Vallancien reported on its feasibility and reproducibility.[3] Additional reports followed, documenting efficacy, and safety, similar to the open approach.[4,5] Furthermore, the advantages of this minimally invasive approach were brought to the fore, increasing the appeal of such procedures for both patients and surgeons. The combination of improved cosmesis, shorter convalescence along with reports of decreased morbidity, and surgical efficiency have led to increased patient demand, resulting in many centers taking a second look at this newer technology.

Despite the publication of large series, until recently the procedure remained limited to academic centers equipped with advanced laparoscopic skills. The proliferation of centers performing laparoscopic or minimally invasive prostatectomy can be attributed to the arrival of the da Vinci robot.[6] Contrasting LRP and robot-assisted radical prostatectomy (RARP), there are many advantages, disadvantages, similarities, and dissimilarities to each technique (Table 18.1).

ADVANTAGES OF LAPAROSCOPIC AND ROBOT-ASSISTED RADICAL PROSTATECTOMY

Enhanced view of the surgical field

When compared with open radical prostatectomy, laparoscopic and robot-assisted radical

Table 18.1 Laparoscopic radical prostatectomy vs robot-assisted prostatectomy

Type of surgery	*Advantages*	*Disadvantages*
Laparoscopic	• Affordable • Reusable instruments • Short set-up times • Easy access to the patient	• No 3D visualization • Reduced tactile feedback • Limited range of motion (4 degrees of freedom)
Robotic	• 3D visualization • Improved dexterity • Increased range of motion (6 degrees of freedom) • Tremor filtration • Ability for scale motion • Ergonomic and untiring • Possibility for telesurgery • Possibility for telementoring	• Very expensive, with high initial investment and maintenance cost • Long set up times • High set-up cost with the need for additional trained staff • Large size of the robot • Highly specialized instruments • No tactile feedback • Remote surgeon location

prostatectomy are often praised for offering both patients and surgeons significant advantages. The laparoscope provides a magnified view of the targeted organ. With a magnification 10–15× that of the unaided eye, the surgeon can visualize fine anatomical details that theoretically increase precision. Magnifying surgical glasses used by some open surgeons only provide a 2–5× that of the unaided eye. In a narrow pelvis, it may often be difficult to visualize all aspects of the prostate due to the surgeon's or assistant's hand retracting or carrying out different steps in the procedure.

In open surgery, a prominent pubic bone angled downward may obstruct the prostate and may require a pubectomy for proper visualization. Under normal circumstances, the apical aspect of the prostate may also be poorly visualized, which would require the surgeon to place significant traction on the base of the prostate to allow an accurate transection of the urethra, to decrease the risk of a positive apical margin. This can also compromise the vesicourethral anastomosis as the transected urethra retracts further behind the pubic bone. During LRP or RARP, the surgeon can position the camera within centimeters of the prostate, allowing an unparalleled view of anatomical details necessary to complete the procedure.

In contrast to pure laparoscopic radical prostatectomy, robot-assisted radical prostatectomy carries the advantage of three-dimensional (3D) visualization, which further enhances the surgical field. The da Vinci robot is equipped with a dual 3-chip camera system, which allows high-resolution immersive stereo display of the surgical field. With the activation of a pedal, the surgeon is able to focus or move the camera, eliminating the need for additional personnel to perform that task as directed by the surgeon. In LRP, a monocular camera is used to provide a 2D view, which contributes to poor spatial and depth perception, and can lead to impaired hand–eye coordination. Newer head-mounted systems (Karl Storz, Germany, and Viking Systems, LaJolla, CA) are available to provide a 3D view of the surgical field during LRP. These devices are routinely used at many centers, and remain promising, but the views provided do not rival those of the da Vinci system.

Enhancing a surgeon's dexterity

With LRP, there is significant reduction in a surgeon's range of motion. The trocar is fixed in its position on the abdominal wall, limiting the surgeon's movement to only 4 degrees of freedom. The only motions possible with the port fixed at the abdominal wall are rotation, pitch, yaw, and insertion. Robotic systems, however, have articulation at the tip of the instruments, allowing an additional 2 degrees of freedom. The articulating tips of the instruments mimic the human wrist and allow the surgeon to work in many different planes. The computer interface provides tremor filtration, and motion scaling not available during LRP. This contributes to increased precision with fine surgical maneuvers. The movements of the operating console surgeon can be translated into micromovements inside the patient. The da Vinci robot allows 1:1, 1:3, and 1:5 scaling. For example, if the motion scale is set at 3:1, every 3 cm motion at the surgeon console will translate into 1 cm motion inside the patient.

During laparoscopic or open prostatectomy, the surgeon stands at the patient's side to carry out the procedure. With robot-assisted surgery, the surgeon sits comfortably at the console, with forearms and head rested. The ergonomic positioning contributes to decreased surgeon fatigue, facilitating the procedure. This is at the expense of being remote from the patient, unscrubbed, and possibly unable to respond to an emergency situation in a timely fashion. Another drawback related to the remote positioning is the inability of the surgeon to put all his senses to use, particularly the sense of touch, which will be discussed later.

Decreased blood loss

Blood loss is significantly reduced during laparoscopic or robot-assisted surgery, therefore decreasing the need for blood transfusions. Bleeding from small capillary vessels is virtually eliminated with the use of carbon dioxide to increase intra-abdominal pressure necessary to create the working cavity. A pressure of 12–15 mmHg serves to tamponade small vessels' oozing, which is generally responsible for bleeding during open prostatectomy. In cases of bleeding from larger vessels such as the dorsal vein complex, the pressure can be temporarily increased further to allow control of the bleeding vessel. Such a maneuver should be very short, with the pressure not exceeding 20 mmHg, to avoid the risk of air embolus and its potential complications. With the decreased need for blood transfusion, donation of autologous blood prior to surgery in anticipation of intraoperative bleeding is no longer advised, a practice which has been routine in many open prostatectomy practices.

Shorter convalescence

With the advent of prostate-specific antigen (PSA), prostate cancer is increasingly diagnosed in younger men, who seek a treatment that is the least disruptive to their active lives. The laparoscopic approach is appealing in that it is associated with shorter recovery. The small incisions used heal rapidly, and allow patients to return to their normal preoperative activity level within a few days. A decreased pain medication requirement is associated with rapid discharge, with a number of series reporting discharging their patients home within 24 hours after surgery.[7] In the USA, patients are discharged with the Foley catheter in place, whereas in Europe they are often kept in the hospital until the catheter is removed, accounting for the different lengths of hospital stay reported.

With laparoscopic surgery with or without robotic assistance, catheterization time has decreased from 1–3 weeks for open surgery to 3–7 days. The enhanced magnification of the surgical field and the ability to place the camera behind the pubic symphysis, as described above, allows direct visualization of the vesicourethral anastomosis. A watertight anastomosis results in faster healing and permits early catheter removal.

DISADVANTAGES OF LAPAROSCOPIC AND ROBOT-ASSISTED RADICAL PROSTATECTOMY

Despite the advantages of laparoscopic surgery, there remain barriers preventing its widespread adoption. Laparoscopic prostatectomy is very challenging and is associated with a very steep learning curve. During the last 6 years there have been significant advances in the field of laparoscopic prostate surgery, particularly the addition of the da Vinci surgical system. A number of surgeons untrained in laparoscopic technology have embraced robotic prostatectomy, reporting success comparable to pure laparoscopic and open prostatectomy approaches.[6,8]

Learning curve

Surgeons experienced in open prostatectomy procedures have made a smooth transition to robotic prostatectomy, while pure laparoscopic prostatectomy remains beyond their reach. The number of cases taken to perform a robotic prostatectomy in 4 hours, or the '4-hour learning curve', has been estimated at 15–30 cases for experienced open surgeons. This number, however, increases to 60–100 cases for surgeons switching from open to pure LRP.[6,8] Although the learning curve remains a highly debated topic, there most likely will never be a consensus as to what the learning curve is for each procedure, as every surgeon embarks on these procedures with varying skill levels. One must also caution regarding the overall skill set available at the institutions publishing these learning curve numbers. These institutions are equipped with surgeons skilled in laparoscopic procedures, who are actively involved in proctoring these laparoscopic naïve surgeons through their learning phase.[6,8]

Movements during laparoscopic surgery are counterintuitive. To reach a structure on the patient's right, the surgeon must move his hand to the patient's right or vice versa. Laparoscopy requires different hand–eye coordination or movements compared wih open surgery. Robotic instruments eliminate these limitations. The placement of trocars to perform robotic prostatectomy, however, requires the acquisition of proper laparoscopic skills. Basic laparoscopic skills are necessary prior to embarking on a robotic prostatectomy program. This is most essential for the bedside assistant involved in passing instruments in and out of the patient. The 'see one, do one, teach one' model, which did not apply to open radical prostatectomy, also does not apply to laparoscopic or robotic prostatectomy. Radical prostatectomy, regardless of the approach, remains a complex procedure, that can be associated with significant complications. Skills acquisition by both surgeon and assistant as a team is necessary to develop a successful laparoscopic or robotic prostatectomy program. We recommend formal training through fellowship, or preceptorship, with case observation to facilitate skills transfer.[9]

Instrument set up

Once the trocars are in place, the surgeon performing an LRP can immediately proceed with removal of the cancerous prostate. With robot-assisted prostatectomy, trocar placement is followed by connection of the surgical cart to the patient. The surgeon then removes his surgical gowns and gloves, and proceeds to the surgical cart to begin the operation. Instrument set-up time is relative to the center's experience. Set-up times have been reported to be as long as 1 hour for centers early in their experience. At our center, we have had set-up time, or time from skin incision to robot docking, of less than 10 minutes with increasing experience.[7] The newer da Vinci 'S' unit has been marketed as having faster set-up times, from quick cannula attachment, in addition to easier instrument exchange. This has yet to be reported in the peer-reviewed literature. The size of the da Vinci unit, and the mobility of the 'spider-like' surgical arms, have been reported as causes for prolonged set-up times. The new unit has been miniaturized, and motorized to facilitate movement, but the machine remains large, and can be cumbersome in today's overcrowded operating room.

Losing the sense of touch

During LRP, the surgeon stands at the bedside, which allows preservation of tactile sensation, albeit much decreased when compared with open surgery. With the lack of a computer interface, the laparoscopic instruments are a direct extension of a surgeon's hands, similar to instruments used during open surgery. Differences in tissue texture, consistency, or suture tension can be appreciated. This is in contrast to RARP, where the surgeon completely loses the sense of touch. The surgeon is completely unaware of the force of the instruments, or the amount of tension placed on tissues, or sutures. This is most evident when a surgeon uses too much tension to tie a knot, which often leads to suture rupture. Currently, even in the newly available da Vinci 'S' model, the technology to allow the surgeon tactile feedback based on contours and textures of tissue has not been added.

The lack of proprioception and tactile feedback remain significant impediments, which perhaps unnecessarily lengthen the learning curve for robotic prostatectomy. Opponents of laparoscopic or robotic prostatectomy often point to this, citing the ability to palpate the prostate and differentiate between cancerous and normal prostate tissue. Historically, this was most useful when prostate cancer was diagnosed at locally advanced stages. Palpation and blunt dissection were used to identify proper planes to allow excision of all cancerous tissues. In the PSA era, where the majority of patients present early with unpalpable disease, the advantage of tactile feedback remains theoretical in allowing the detection of cancerous tissue. Pathological assessment remains the only way to diagnose disease extension outside of the prostate capsule.

The cost factor

Unlike the da Vinci robot, the instruments used to perform laparoscopic prostatectomy are generally non-disposable. LRP instruments can be used until the surgeon decides they are unsuitable. The number of times a surgeon uses a da Vinci robot instrument, however, is predetermined by the manufacturer. Instruments are electronically disabled after a certain number of uses. This set number, perhaps necessary to allow the robot to be used safely, is responsible for the cost premium associated with RARP.

Besides instrument cost per case, both LRP and RARP are associated with initial costs, and maintenance costs, which are much higher for the latter. With LRP, the Automated Endoscopic System for Optimal Positioning (AESOP) is often used, which cost nearly US $200 000. Purchasing costs of the da Vinci robot and the newer da Vinci 'S' are US $1.3 million, and US $1.7 million, respectively. Annual maintenance costs of the da Vinci robot are estimated at US $250 000.

When comparing the cost of open vs laparoscopic and robotic prostatectomy, Lotan et al reported the robot-assisted approach to be the most costly.[10] Excluding the cost of purchasing the da Vinci robot, RARP was found to cost US $1155 more than open prostatectomy. LRP in turn costs US $533 more than the open approach.[10] A more recent study by Scales et al reported RARP to be cost competitive with open prostatectomy at centers performing 14 cases weekly.[11] The volume-based cost competitiveness, however, was calculated from shorter length of stay (LOS) associated with the robotic prostatectomy approach. Both LRP and RARP have a similar length of stay of 1–2 days. Performing a large number of cases does not allow a center to gain a cost advantage with RARP. The cost per case is unchanged, preventing a center from gaining benefits associated with economies of scale. We have found RARP to be more expensive than LRP, due to recurring high disposable costs.[12] Experience effects also do not have an impact on the cost of robot-assisted prostatectomy, owing to the high costs of disposables and reposables. For a center already skilled in performing LRP, there is no cost buffer due to further decrease in LOS, by switching to a robot-assisted approach. The da Vinci robot will remain unaffordable to many centers because of the high initial investment, per case, and maintenance costs.

OUTCOMES OF LAPAROSCOPIC RADICAL PROSTATECTOMY VS ROBOT-ASSISTED PROSTATECTOMY

Since the initial reports by Guillonneau et al on LRP,[3] and those by Menon on RARP,[6] a number of studies have been published reporting varying results with different techniques. Different methodologies or approaches have made these studies difficult to compare. Some surgeons use a transperitoneal laparoscopic approach, whereas others prefer an extraperitoneal route. There is no randomized prospective study published comparing LRP to RARP. There is also no published randomized study exploring whether an extraperitoneal approach is more advantageous than the transperitoneal approach.

Extraperitoneal LRP is generally associated with a shorter operative time. Mean operative times for transperitoneal LRP and extraperitoneal LRP have been reported to be 224 minutes and 168 minutes, respectively.[13–15] The extraperitoneal approach may very well offer a time advantage, but this may be the result of a learning-curve effect. Most centers embark on the extraperitoneal approach after an initial experience with the transperitoneal approach. For RARP, mean operative time for several major series ranges from 141 to 558 minutes.[16–18] Ahlering et al found no significant difference between the time required for RARP (231 minutes) and open radical prostatectomy (214 minutes).[17] Our center is one of the few worldwide to have converted from LRP to RARP. Comparing consecutive series of 50 cases of LRP and RARP, the mean surgical times for LRP and RARP were 235 and 202 minutes, respectively.[9] Our robotic series probably benefited from the learning curve of our LRP series. Operative times for each approach vary significantly. They are dependent on the surgeon's experience and are difficult to interpret, and perhaps should not be used to compare one procedure with another.

Both LRP and RARP have been shown to be comparable to open prostatectomy when basic oncological principles are reviewed. Positive surgical margin rates can be used as a marker of oncological efficacy. We found no significant difference in the positive surgical margin rates in our study comparing LRP vs RARP.[9] For LRP, the reported mean positive margin rate is 19.2% (range 15–30%), with no difference reported between the extraperitoneal or transperitoneal approach.[13,15,19] Mean positive surgical margin rate for RARP is 11% (range 6–30%).[16–18] Besides our center, none of the centers reporting these rates routinely perform both LRP and RARP. These varying results point to the paucity of studies comparing the two approaches in an objective fashion. Prospective studies are needed to ascertain whether RARP provides true advantages.

CONCLUSIONS

Whether a radical prostatectomy is performed using a pure laparoscopic or a robot-assisted approach, the goal remains the same – to eradicate the cancer while preserving anatomical structures necessary to maintain continence and potency. Both LRP and RARP allow the procedure to be performed with less blood loss in a minimally invasive fashion, therefore becoming increasingly attractive options. For LRP and RARP to change the status of the gold standard open prostatectomy, they must not only show equivalency but also superiority. Long-term results are needed that show achievement of these goals, with reduction of the morbidity associated with open radical prostatectomy.

The use of the robot is associated with both advantages and disadvantages. In Europe LRP is more commonly performed, whereas in the United States RARP is a more popular procedure. RARP is more costly than LRP, which limits its adoption worldwide. At the University of Rochester Medical Center, robot-assisted extraperitoneal radical prostatectomy has become our preferred and most commonly performed procedure to remove a cancerous prostate. In our hands, this approach offers equivalent oncological results, with decreased transfusion rates, shorter convalescence, and excellent functional results.[7]

The robot adds to a surgeon's dexterity, theoretically increasing the precision of surgery; it remains an ultimate application of technology in the surgical management of prostate cancer. The use of the robot, and soon microrobot, to assist in laparoscopic prostate surgery is here to stay.[20] The staggering cost of the da Vinci robot, in addition to the development of laparoscopic equipment with articulating joints and head-mounted 3D viewing systems, will continue to challenge the use of the robot, particularly in government-sponsored health systems with a cost-containment orientation, in the quest for a new gold standard.

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Part 6: Postoperative considerations

CHAPTER 19

Postoperative care of the patient

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INTRODUCTION

Over the last two decades, dramatic improvements have occurred in postoperative care of patients undergoing radical prostatectomy (RP). The reasons for these advances are multifactorial and include better patient selection, improved perioperative management, refinements in surgical techniques and experience gained through the development, and continuous reassessment of clinical pathways. The overwhelming majority of lessons learned over the past decade were derived from the management of patients undergoing radical prostatectomy via an open, retropubic approach and to a lesser extent via a perineal incision.

Laparoscopic techniques with or without the assistance of robotics are now being offered with increasing frequency. Interestingly, the postoperative management of patients undergoing laparoscopic and open radical prostatectomy is surprisingly similar, with only minor differences in the patient management in the early recovery period. Furthermore, both the open and laparoscopic techniques have had a synergistic impact on modifications of the clinical pathways that have directly and indirectly resulted in reduced morbidity and length of hospital stay.

INPATIENT AND OUTPATIENT MANAGEMENT

Although many of the same basic principles apply in the postoperative care of patients following radical prostatectomy, numerous steps in the management have now been shifted to the outpatient setting. Additionally, many hospitals, particularly those dealing with a high volume of cases, have also established collaborative care pathways to optimize perioperative and postoperative patient care. These advancements in the postoperative care of radical prostatectomy patients have resulted in significantly reduced length of hospital stay and decreased healthcare cost. Most importantly, these adaptations have been accomplished without compromise in patient care or outcomes, and consequently there has been no increased morbidity.

Immediate postoperative period

In the immediate postoperative recovery period (1–6 hours), patient care revolves around monitoring of vital signs, urine output via the Foley catheter, and pelvic drain output. The hospital course after RP is often uneventful and, in that situation, typically there is no laboratory evaluation that is necessary in the immediate postoperative period. In the event of significant sanguineous drain output, gross hematuria, or unstable vital signs, laboratory evaluation with hemoglobin or hematocrit should be performed immediately to establish a new baseline and to determine the need for transfusion and further testing.

From the recovery room, RP patients are sent to a regular hospital floor routinely without the need for invasive monitoring. Although a majority of prostatectomy patients do not require special monitoring, if significant comorbidities or circumstances exist, care must be taken to ensure that patients are sent to a setting that is appropriate for the desired level of care. Thus, a small percentage of patients may require a cardiac monitoring unit or an intensive care unit, depending on the particular situation.

Proper assessment of fluid status after the operation should be made and addressed with bolus intravenous fluids and/or blood products given as needed. If significant postoperative bleeding occurs, several steps may be employed to help reduce bleeding from the prostatic fossa. In the setting of gross hematuria, gentle traction can be applied to the Foley catheter after instillation of 30–50 ml of saline solution in the balloon. Manual bladder irrigation may also be instituted if hematuria persists or clot formation occurs. If significant bleeding from the insertion site of the drain is noted, a computed tomography (CT) scan should be obtained to attempt to identify the source of the bleeding: this includes bleeding from the pelvic vessels, the inferior epigastric vessels, or the dorsal venous complex. On rare occasions, the bleeding will be such as to necessitate a take back to the operative room for re-exploration. Fortunately, the reoperation rate for active bleeding is exceptionally low, at less than 0.5%.[1]

Fluid and electrolyte management

During the immediate postoperative period, all RP patients should initially be on intravenous (IV) fluids. Resuscitative fluids with 0.9% normal saline (NS) or lactated Ringer's solution in the immediate postoperative period are commonly employed. On postoperative day 1, the fluid may be switched to maintenance IV fluids of D_5 0.5 NS with 20 mEq potassium chloride. Electrolyte abnormalities are not common in this setting, but if symptoms or comorbidities exist, proper adjustments in IV fluids should be made and electrolyte evaluation may be warranted.

Laboratory evaluation and postoperative bleeding

Routine preoperative evaluation and a hematocrit on the morning of postoperative day 1 are considered standard and our preferred management, as outlined in the clinical pathway. Other laboratory evaluations may be necessary but are not performed routinely. Although transfusion rates for both open RP and robot-assisted laparoscopic prostatectomy (RALP) are now fortunately quite low, one of the well-recognized complications during RP is acute blood loss anemia. Transfusion rates in the past were as high as 69%, but over the last few decades, with techniques described by Walsh and others that allow for control of the dorsal venous complex, only 2–11% of patients undergoing radical prostatectomy required transfusion.[2,3] Transfusion of packed red blood cells has been shown to reduce perioperative mortality if the hematocrit is less than 27% in patients with recent myocardial infarction and less than 21% in other patients.[4] It has also been shown that the preoperative hematocrit may be predictive of the need for a transfusion.[5,6]

Diet

In a majority of collaborative care pathways after RP, early advancement of diet has been adopted. RP patients are often advanced to a clear or full liquid diet on the evening of surgery. Because of the extraperitoneal approach and minimal bowel manipulation, open RP patients may be advanced to a solid diet before hospital discharge and prior to the return of bowel activity. RALP patients are often continued on a liquid diet until the return of bowel function and may be discharged home on a liquid diet. Some urologists still advocate return of bowel function before advancement of diet, despite the surgical approach. For this reason, it should be noted that diet advancement should ultimately be at the discretion of the treating physician.

Activity and DVT prophylaxis

All patients should be encouraged to ambulate, often with assistance, in the postoperative period. Early ambulation in orthopedic hip replacement surgery has been shown to reduce the incidence of venous thromboembolism and lung atelectasis and has been implemented in the care of many urological surgical patients.[7,8] Institution of physical and/or occupational therapy is typically unnecessary.

Pre- and postoperatively RP patients are routinely placed in antiembolism stockings and sequential compression devices (SCD) to reduce deep vein thrombosis (DVT) formation. The use of perioperative DVT prophylaxis with heparinoids is controversial and unclear. In a recent consensus statement on the prevention of venous thromboembolism, the American College of Chest Physicians compiled a comprehensive review of the literature and offered recommendations to define evidence-based guidelines for DVT prophylaxis for major urological surgery.[9] Additionally, these guidelines did take into account that there is a higher incidence of DVT in cancer patients.[10] Specific recommendations for urological surgery revealed that use of antiembolism stockings and SCD and/or heparinoids reduces thromboembolic events. Whether to institute the use of one or multiple combinations is based on the presence or absence of other comorbidities, presumed bleeding, and surgical technique. Recent literature addressing urological laparoscopy revealed increased hemorrhagic complications associated with use of fractionated heparin without a reduction of thrombotic complications compared with SCD.[11] Currently, we do not routinely use fractionated heparin in our collaborative care pathway for RALP patients but do for our open RP patients.

Postoperative medications

Pain control after RP is usually achieved through the use of narcotics, IV in the immediate postoperative period, with the addition of oral agents when patients can tolerate a liquid diet. Patient-controlled analgesia pumps are often unnecessary and, in fact, have now been removed from our routine clinical pathway for both open and laparoscopic approaches. Nonsteroidal anti-inflammatory drugs (NSAIDs), in the form of IV ketorolac tromethamine, may also be utilized if there are no contraindications to its usage and no evidence of active bleeding. Patients are often prescribed oral narcotic pain medication on discharge and instructed to take laxatives or stool softeners, to prevent the constipating effects of narcotic use.

Shortly after general anesthesia, nausea and vomiting is not uncommon. Antiemetics, as selective 5-HT$_3$ receptor antagonists and some antihistamines such as promethazine, reduce perioperative nausea and vomiting.[12] Promotility agents such as metoclopramide have not been shown to prevent postoperative nausea and vomiting.[13] Preoperative steroids have also been shown to reduce postoperative nausea in certain surgical patients and also may be of benefit.[14]

Only perioperative antibiotics within 60 minutes of incision and during the first 24 hours postoperatively have been shown to be beneficial in reducing postoperative infection. Although urological surgery was not specifically addressed, orthopedic, colon, vascular, cardiac, and gynecological surgical infections were evaluated. First- or second-generation cephalosporins are recommended. In cases of allergy to penicillins or cephalosporins, vancomycin and clindamycin are advised.[15]

To reduce perioperative gastric reflux and gastric acid secretion, proton pump inhibitors or antihistamine (H_2 blockers) may be used. Other medications such as perioperative beta blockers may be indicated in high-risk cardiac patients to reduce perioperative myocardial infarction.[16]

Pulmonary toilet

No conclusive evidence has been reported to advocate the use of incentive spirometry (IS).[17] Secondary to the low cost, IS devices are used routinely to promote deep breathing and assist in pulmonary toilet. Not only does IS result in lung expansion but it also promotes patient self-care and may be performed by an outpatient. Care of patients with severely compromised pulmonary function may necessitate more aggressive pulmonary therapy, including supplemental oxygen, percussion therapy, and intermittent positive pressure breathing or inhaled nebulizers.

Catheters and drains

At our institution, all RP patients have both a urethral catheter and a closed, suction pelvic drain. Some surgeons advocate assessing the patency of the anastomoses intraoperatively and, if there is no evidence of extravasation, safely omitting the use of a drain.[18] During hospitalization, accurate output from the urethral catheter may be achieved by the use of a urine meter bag, with emptying and recording every 8 hours; the catheter may be irrigated if necessary. Proper securement to the thigh is necessary to ensure that the catheter is not accidentally dislodged. As nearly all patients are discharged home with the catheter, careful instruction by trained staff is given in the management of the catheter as per standards during the hospitalization.

Routinely, urethral catheters are removed after 7–14 days. Some authors endorse early catheter removal with cystographic evaluation prior to removal to assess for urinary extravasation.[19] Other groups advocate catheter removal without evaluation by cystography as early as postoperative day 4 with low rates of acute retention or long-term complications; however, this is countered by studies which have revealed higher rates of retention with earlier catheter removal.[20–23] Several groups have shown acute urinary retention at 1.3% in patients with catheter removal between 6 and 14 days postoperatively, also without the use of cystograms.[24,25]

The pelvic drain should be monitored for the character of the output (sanguineous, serosanguineous, serous, etc.) as well as the amount. The drain should be stripped, emptied, and recorded at least every 8 hours and as needed. A vast majority of patients have the pelvic drain removed prior to discharge unless significant output is noted. For open RP, output of less than 50 ml per shift is considered appropriate for removal. Owing to the intraperitoneal approach of most laparoscopic techniques, the output from drains is normally higher secondary to peritoneal fluid, and removal is decided by the surgeon on a case-by-case basis. If concern exists over the content of the fluid, a creatinine level reading from the drain fluid should be sent and compared with the creatinine of the serum. In cases of significantly elevated creatinine concentration in the drain fluid, a urine leak is confirmed and the drain is left in place until the leak is sealed.

If patients are sent home with a pelvic drain, careful instruction on proper care should be given during the hospitalization. Usually, patients are instructed to record the output for a 24-hour period. Drains are then removed in the outpatient setting when output has declined to suitable amounts, as mentioned previously. Any gauze dressing or the like is often kept in place for 1–2 days after surgery and may be removed during hospitalization or at home. The use of absorbable sutures or staples is commonplace; staples are normally removed after 10–14 days.

Length of stay

The average duration of hospital stay has dramatically decreased over the last few decades. The motive for shorter hospital stays has been the ever-increasing healthcare costs. In recent reports, > 95% of RALP patients are discharged within the first 23 hours postoperatively. At our institution, with increasing numbers of RALP patients, hospital stays have declined from a 2-day length of stay (LOS) to 1.3 days. In addition, we have appreciated shorter LOS for open RP patients without a significant increase in postoperative complications or readmission rates. Some patients undergoing perineal RP have been treated on an outpatient basis.[26] However, most patients not managed under the guidance of a collaborative care pathway continue to stay in the hospital for 2–3 days after open RP, although this trend is decreasing as more data regarding efficacy emerge.

COLLABORATIVE CARE PATHWAYS

With the current healthcare environment, cost containment is of the utmost importance. Many academic institutions have designed collaborative care pathways to help assist in the escalating costs of health care, while still providing state-of-the-art medical care. These pathways provide an outline to streamline perioperative management by reducing duration of stay and hospital costs. Collaborative care pathways institute evidence-based medical care with less emphasis on the surgeon’s own experiences and habituations. These evidence-based order sets provide guidelines for length of stay, laboratory evaluation, proper advancement of diet and activity, and pain medications. Table 19.1 shows an example of pathway orders for both open RP and RALP at one major urological institution.[27]

CONCLUSIONS

Over the past decade, there have been dramatic improvements in the postoperative management of patients following radical prostatectomy. These refinements are applicable to both open and laparoscopic approaches, and in most cases the postoperative management is similar. The use of collaborative care pathways has allowed for continued modifications and improvements in the management of these patients without compromising patient care or outcomes. The incorporation of evidence-based medicine into these pathways should allow for continued improvements based on scientific rationale rather than anecdotes.

Table 19.1 RRP and RALP pathways

	Open RP	*RALP*
Preoperative	1. Enoxaparin 40 mg subcutaneously 2. Cefazolin 1 g IV 3. Graduated compression stockings 4. Intermittent pneumatic compression 5. Hematocrit 6. Bowel prep	Same as open RRP except no enoxaparin

Continued

Table 19.1 RRP and RALP pathways–cont'd

	Open RP	*RALP*
Care reminders and treatments	1. Vital signs q4h × 24h, then q8h 2. Strict in/outs q4h 3. Catheter to bedside bag 4. JP drain to bulb suction 5. Turn/cough/deep breath q1h + incentive spirometry q1h 6. Graduated compression stockings 7. Intermittent pneumatic compression 8. NHO for T >101.5; SBP <90 >160; DBP >100; P <60 >120; UOP <150 cc/4h	Same as open RRP
Diet	1. NPO with no ice chips 2. Full liquid diet at breakfast POD # 1 + regular diet at lunch on POD # 1	Same as open RRP
Laboratory	Hematocrit in a.m. POD # 1	Same as RRP
Catheter removal	10 days postoperatively	Same as RRP

From the collaborative care pathway utilized at Vanderbilt Unversity Medical Center, Department of Urologic Surgery.
SBP, systolic blood pressure; DBP, diastolic blood pressure; NHO, notify house officer; NPO, nothing by mouth; T, temperature in degrees Farenheit; P, pulse; UOP, urine output; POD, postoperative day; JP, Jackson-Pratt.

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CHAPTER 20

Assessment of radical prostatectomy specimens and pelvic lymph nodes

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The incidence of prostate cancer (PCa) has risen dramatically in the past decade, probably owing to early detection programs that employ digital rectal examination, serum prostate-specific antigen (PSA), and transrectal ultrasonography.[1,2] The increase in PCa detection has induced a sharp increase in the number of radical prostatectomies.[1,3–7] The popularity of surgical treatment is due in part to improvements in technique that decrease the risk of impotence, including nerve-sparing prostatectomy.[8]

One of the main issues for pathologists is the identification in radical prostatectomy (RP) specimens of those prognostic factors that could predict accurately patient outcome. Proper examination of RP specimens is critical in accurately determining the prediction of patient outcome.

HANDLING OF RADICAL PROSTATECTOMY SPECIMENS

Radical prostatectomy gives the most accurate and detailed information available for determining prognosis and deciding about adjuvant therapy for prostate cancer. Consistency and reproducibility of observations from these specimens requires a standardized protocol for tissue fixation, sampling, embedding, and processing.

Initial handling of radical prostatectomy specimens

When RP specimens arrive in the laboratory, pathologists and trainee assistants should inspect the organ promptly. Topography, surgical procedure, and fixation status should be noted in the record. The surgical team should be contacted if any of these properties is uncertain. Specimen identification, including patient's name and medical record number, should be verified (Table 20.1).

The fresh (unfixed) RP specimen is weighed and may be measured in three dimensions: width, height, and length. The volume of the specimen is calculated as the volume of an ellipse:[1]

$$(\text{Width} \times \text{Height} \times \text{Length}) \times 0.523$$

Although recording the weight of RP specimens is important for documentation, especially when supplemented by comments related to the completeness of resection, the value of recording dimensions in addition to weight is of less obvious value. Because the resected

Table 20.1 Clinical information

1. Patient identification
   1. Identification number
   2. Name
   3. Age (birth date)
2. Clinical information
   1. Relevant history and preoperative findings (previous diagnosis, treatment, including PSA, imaging)
   2. Operative findings
   3. Anatomical site(s) of specimen(s)
   4. Procedure:
      - Retropubic procedure:
        nerve sparing
        standard radical
      - Perineal procedure
      - Open RP, laparoscopic RP and robotic RP
3. Responsible physician(s)

prostate is an irregular structure, symmetric in only one axis – about the sagittal plane – linear measurements are less accurate and reproducible than specimen weight.

Gross examination of specimens

The specimens must be well-oriented. If difficulty arises in orientation, the pathologist should contact the urologist for clarification. The entire specimen is carefully inspected and palpated to localize zones of nodularity or induration. If there is asymmetry or a palpable abnormality, the location, size, and texture of the lesion should be recorded. Previous reports of needle biopsy or transrectal ultrasound should serve as aids to identifying the location and size of the tumor.

Fixation and inking

To enhance a quick and uniform penetration of the fixative, the prostate specimen is injected with 10% neutral-buffered formalin solution using a fine hypodermic needle (0.6 × 25 mm, for instance). After plunging the needle deep into the prostatic tissue, formalin solution is slowly injected while the needle is slowly retracted. Formalin injection is performed in a systematic way, at multiple 0.5 cm spaced sites at all sides of the RP specimen. In total, approximately 100 ml of formalin solution is injected (for details see Ref. 9). This procedure does not lead to damage to the morphology of the prostatic tissue. The rationale behind the injection procedure is that, during immersion in a formalin solution, the fixative only slowly diffuses toward the center of the specimen. When the periphery of the prostate is fixed, the presence of cross-linked proteins is thought to hinder further diffusion of the fixative toward the center of the specimen (so-called crust-effect).

The entire surface of the RP specimen is inked using two different colors for each side in order to recognize the left and right. Green and red (or blue) are usually used. By immersing the inked gland into a mordant, such as Bouin's solution or acetic acid, the ink is fixed to the surface. India ink could be preferred to the two-color-procedure because the black-colored margins are more easily identified when the sections are examined under the microscope. Inking is important because the surface of the prostate is fibromuscular tissue that does not form a discrete histological boundary with extraprostatic, pelvic soft tissue. Because proximity of tumor to margin cannot be predicted based on the gross appearance of the cut surface of the prostate, the entire surface should be inked. Inking each side with a different color helps retain orientation as sections are obtained and provides a cross-check for section location.

The RP specimen is then immersed in 300–400 ml formalin solution and allowed to fix for 24 hours.

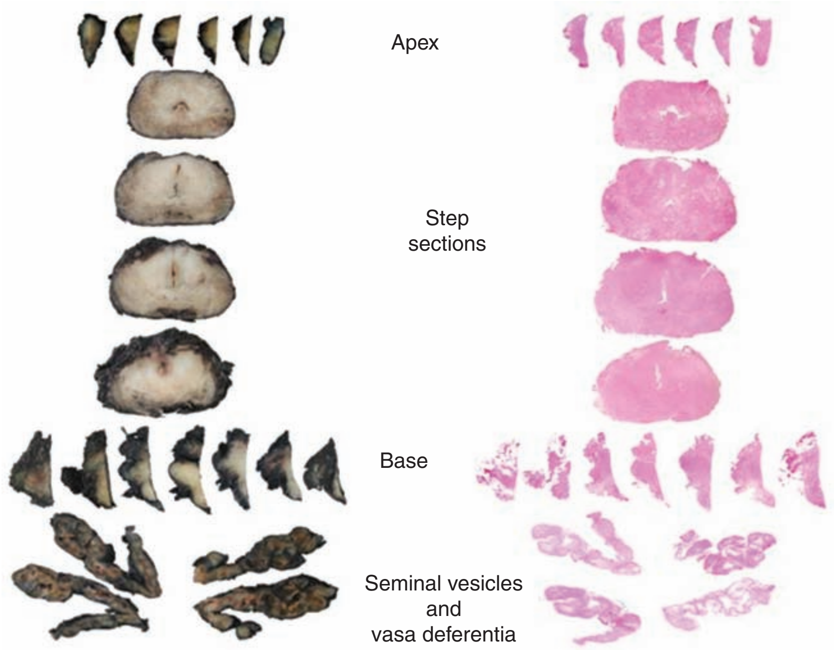

Figure 20.1 Serial coronal sections, parallel to an initial en-face section of the apex, the apical and proximal parts and the seminal vesicles (left). The corresponding histological sections are also shown (right). (Reproduced from Montironi et al,[10] with permission.)

Sectioning (Figure 20.1)

The seminal vesicles (SVs) are amputated at the junction between the base of the seminal vesicles and the prostate surface. Each SV is cut into two halves with a 'sandwich' technique.

The apical and basal parts of the prostate are removed by a transversal cut at 4 mm from the distal and proximal margins, respectively. Optionally, the distal urethral margin may be removed from the apical part and examined separately. The apical and proximal parts are then sectioned as follows: slices are cut parasagittally at 3 mm intervals and perpendicularly to the inked surface. An alternate method would be to section in a radial fashion, similar to the cutting of a cone biopsy of the uterine cervix. Whatever the method of cutting, all margin sections are microscopically examined. Some pathologists prefer shave margins to sample a larger surface region and to disclose the two-dimensional extent of margin exposure. They take thin margin specimens of 1–2 mm thickness on the surface of apex and bladder neck.[11,12] If any cancer cell is identified in the shave specimens, the margin is regarded as positive. Although this method avoids missing a tiny positive margin between the margin sections of perpendicular sampling, the thicker shave section may artificially result in a false-positive histological margin (Figure 20.2).

The prostate specimen is step-sectioned at 3 mm intervals perpendicular to the long axis (apical–basal) of the gland. A slicing machine should be used. Serial coronal sections, parallel to an initial en-face section of the apex, are

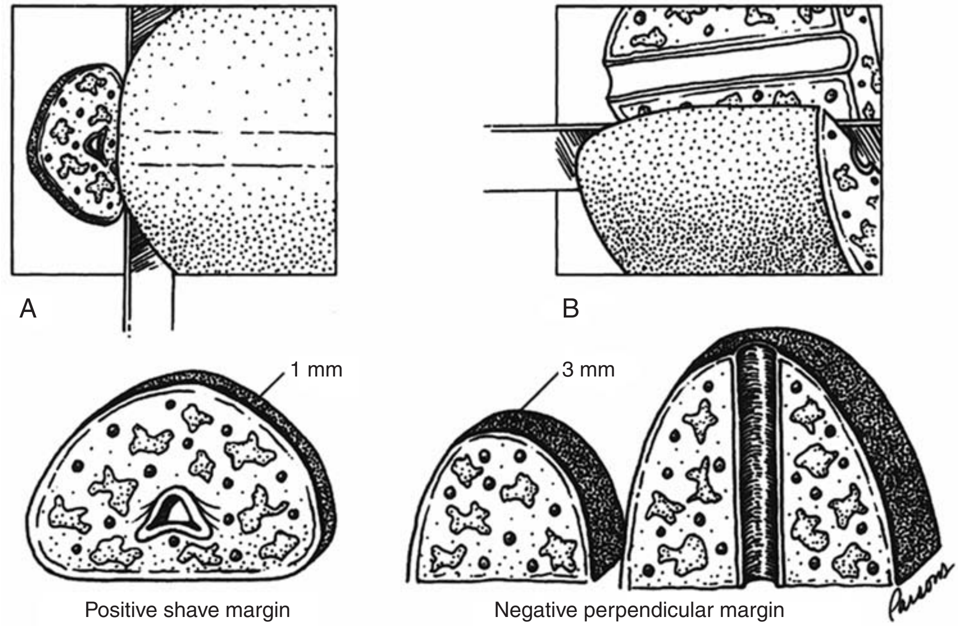

Figure 20.2 Different techniques of processing the apical margin in the same case where there is tumor at the apex. Small circles represent cancer. Larger irregular spaces represent benign glands. (Reproduced from Epstein et al,[11] with permission.) (A) A shave margin of the apical margin consists of a thin (1 mm) slice perpendicular to the urethra. The entire section is considered the margin, regardless of whether the tumor extends to the inked edge of the section. The case would be signed out as showing a positive margin (?), as both cancer and benign glands are at the margin. (B) Perpendicular margins consist of serial thicker (3 mm) slices parallel to the urethra. Only the inked edge of the section is considered the margin. The case would be signed out as showing organ-confined disease with negative margins and no capsular incision, as both benign glands and cancer do not extend to the inked edge of the section.

taken until the junction of the seminal vesicles is approached. The whole-mount sections are identified in a consecutive manner with capital letters, always starting from the most apical section. In this way, the whole RP specimen is available for histological examination, as originally described by Stamey et al.[13] When India ink is used, a cut is made with a scalpel in the right anterolateral aspect of each slice to mark the right side.

The transverse sections of prostate should be carefully examined for grossly identifiable cancer (Figure 20.3). Unlike other malignant cancers, in which tumors form a distinct, firm mass, prostate cancers often have similar consistency and color to the surrounding benign tissue. Prostate carcinoma appears as solid gray to yellow-white mass, with wide variation in gross appearance. Grossly apparent tumors are usually at least 5 mm in greatest dimension, and have a firm consistency due to tightly packed neoplastic glands or desmoplastic stroma. The color may be yellow-white due to tissue necrosis and membrane lipid accumulation. In addition, they are often more solid and homogeneous than the surrounding multinodular benign tissue. Some cancers appear

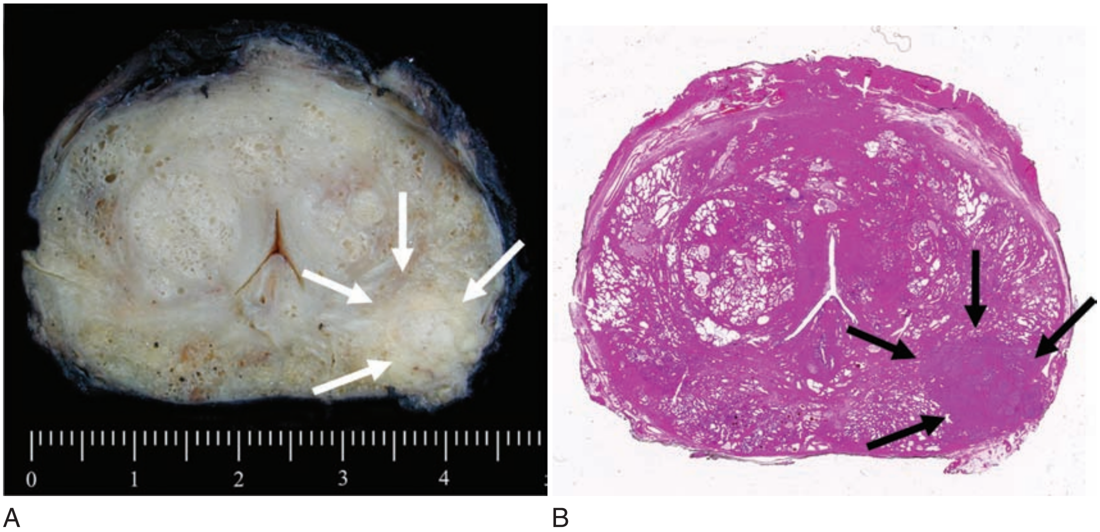

Figure 20.3 Macroscopic identification of areas of prostate cancer. (A) Slice of the body of the prostate gland. An area highly suspicious for cancer is identified macroscopically in the peripheral zone (arrows). (B) Whole-mount section. The arrowed area in the peripheral zone is prostate cancer and corresponds to the area seen in the slice of prostate shown in Figure 20.3A.

as a yellow granular mass, which contrasts sharply with the normal sponge or microcystic prostatic parenchyma. In cases with less apparent lesions, structural asymmetry is an important clue for tumor identification. Many subtle lesions are recognized best by their contrast with the contralateral lobe. After gross inspection of all cross slices, they are serially laid out on the board and photographed to document the block legend. Figure 20.3 also records the location and appearance of prostatic lesions, which may also serve as a reference image for trainees to become familiar with the gross appearance of prostate cancer.

Sampling and embedding

The cut specimen may be post-fixed for 24 hours. The en-face section is then processed as a single section; alternatively, the en-face sections are submitted as quadrants following a systematic numbering scheme. In particular, the cut specimen is dehydrated in graded alcohols, cleared in xylene, embedded in paraffin, and examined histologically as 5 μm-thick, whole-mount, hematoxylin–eosin-stained sections (see Figure 20.3). Special molding and inclusion cassettes should be used. The slides should be at least 76 mm long × 50 mm wide. Cover-slips of a similar size have to be used.

There is not yet a consensus among pathologists as to whether the whole gland should be embedded for sectioning. Complete histological examination of all prostatic tissue is usually reserved for research in academic institutes, not for routine treatment of prostate cancer in community hospitals. The rationale for total embedment of the prostate is based on the fact that the gross appearance of the sectioned prostate is an unreliable guide for tumor distribution. In addition, during the PSA era, tumors have become smaller in size and multifocality of cancer is a frequent finding.[14] Whether the greater time and materials involved in prosecting and examining sections of totally embedded prostate is worthwhile is unclear. Even totally embedding a prostate does not mean that the margins will be completely sampled, unless serial sections are made of each block. When adopting the partial sampling strategy for practice, the remaining prostatic sections should be well preserved in the original orientation. Thus, when additional sections are needed, they can be taken from a positively identified location in the gland. If no cancer is identified on the submitted sections or the tumor closely approaches the surgical margin, pathologists should embed other slices for histological examination. When tumor is not readily identified on the slides even after submission of the entire prostate, one should cut deeper sections from all available blocks.

The dilemma of choosing between whole-mount sections and quadrant sections is one of balancing aesthetics and greater ease in examining sections against the cost of time and materials and the logistical problem of storing glass slides and paraffin blocks of unconventional size. The only significant difference in the histopathology of these two different processing methods is that whole mounts are often thicker sections.

One may also submit the entire prostate in conventional cassettes after cutting the transverse slices sufficiently small to fit. Sections are obtained by slicing each transverse section into two halves or four quadrants. This approach, yielding a mean of 26 slides per case, makes the entire radical prostatectomy specimen available on conventional slides for histological examination.

Handling of RP specimens in cases that are pT0

When cancer is not readily identified in the histological slides, the pathologist should proceed as follows:

1. If the prostate is totally embedded, the diagnostic needle biopsies should be reviewed to assess the approximate location of the tumor. Sections of the prostatectomy of this area should be recut after block-flipping;
2. If the prostate was not totally embedded, this should be done. Immunohistochemistry (IHC) should be applied to identify the so-called ‘minimal residual cancer’[15] (see below).

Role of immunohistochemistry

There are two situations where IHC studies can be of help in evaluating RP specimens from patients receiving neoadjuvant hormonal therapy (NHT).[16]

In those cases where the only apparent residual tumor consists of single cells or groups of cells that cannot reliably be distinguished from macrophages, staining for cytokeratin (using a pancytokeratin cocktail), PSA, or prostatic acid phosphatase may resolve this difficulty. Similarly, when cells are seen in the periprostatic tissues or at the surgical margin whose nature cannot be determined, cytokeratin IHC staining can be of value. The routine use of cytokeratins in cases that are pT0 or pT2 has not been assessed and could be an interesting part of a study protocol.

A second potential role of IHC study is distinguishing benign from malignant glands. In general, this is not a major issue, particularly given the propensity for basal cells to appear more prominent after NHT. If this differentiation should be a problem, it is useful that basal cells continue to express high molecular weight cytokeratins after hormonal treatment.[2]

Proliferation markers (PCNA, Ki-67, i.e. MIB-1) have been used in post-radiation therapy biopsies to indicate the clinical significance of residual tumor. The role of these markers in the setting of NHT has not been systematically addressed and represents a further area where studies could be performed in the clinical trial setting.[5]

Sampling for research purposes

Several techniques have been published as to how to obtain fresh prostate tissue for research purposes without compromising assessment of pathological parameters. An issue germane to all techniques is that once the prostate is incised in its fresh state, the more centrally located tissue tends to bulge beyond the plane of sectioning and the inked ‘capsule’ retracts. A number of alternative approaches may be followed. However, before cutting in the specimen, it is mandatory that the prostatectomy specimen is inked.[2]

- To cut the prostate in half in an area where the tumor is suspected. The fresh tumor, which bulges beyond the surface, is shaved off. The radical prostatectomy specimen is then pinned out in order to prevent further distortion.
- To sample the prostate tissue by 14-gauge needles, a 5 mm skin punch biopsy, or a cork borer. The sampling may be performed parallel to the prostatic surface in order to obtain as much tumor as possible. To prevent distortion or identify the sampling sites histologically, the holes can be filled with cork or ink, respectively.
- To do frozen sections of alternate posterior blocks to check margin and extraprostatic extension status, with the remaining frozen tissue used for research purposes. However, tumor often extends close to the edge of the prostate covered by a flimsy layer of connective tissue or adipose tissue, such that accurately determining margins of resection on frozen section is difficult.
- To ‘peel’ the capsule of the prostate along with several millimeters of underlying tumor from the area of suspected gross tumor. This peel is then serially sectioned perpendicular to the inked surface to assess for extraprostatic extension and margins of resection. All of the remaining tumor within the prostate gland beneath the peel can then be used for harvesting.

Regardless of the technique used, it is becoming more difficult to identify gross tumor to harvest fresh prostate cancer tissue at the time of radical prostatectomy with the detection of earlier prostate cancer.

PATHOLOGY REPORTING OF RADICAL PROSTATECTOMY SPECIMENS

The pathology report has to contain prognostically useful data derived from the evaluation of the RP specimen (Table 20.2).

Histological type of cancer

In general, more than 95% of cases of prostatic carcinoma are acinar adenocarcinoma. In recent years, a number of new and unusual histological variants or subtypes have been identified. These variants represent the spectrum of changes which can occur in adenocarcinoma. The biological behavior of many of these variants may differ from typical adenocarcinoma and proper clinical management depends on accurate diagnosis and separation from tumors arising in other sites. It is recommended that subtypes, such as small cell, ductal and mucinous, should be reported if they are noted histologically. Mixtures of different histological types should be indicated.[17]

Histological grade of cancer

The Gleason score assigned to the tumor at radical prostatectomy is the most powerful predictor of progression following radical prostatectomy[18–23] (Figure 20.4).

The Gleason score is the sum of the primary (most predominant) Gleason grade and the secondary (second most predominant) Gleason grade.

Table 20.2 Microscopic evaluation

1. Tumor
    a. Location(s)
    b. Histological type
    c. Gleason score with primary and secondary grades
    d. Extent of local invasion:
        (1) extraprostatic extension
        (2) seminal vesicle involvement
2. Margins (location and extent of margins involved with tumor)
3. Regional lymph nodes
    a. Number (specify location)
    b. Number involved by tumor:
        (1) specify location, if possible
        (2) size of metastatic deposit (i.e. if <2 mm = micrometastasis)
        (3) extracapsular extension, if present
4. Additional pathological findings, if present
    a. High-grade intraepithelial neoplasia (PIN)
    b. Therapy-related changes
    c. Other(s)
5. Metastasis to other organ(s) or structure(s) (specific sites)
6. Other tissue(s)/organ(s)
7. Results/status of special studies
8. Comments
    a. Correlation with intraoperative consultation, as appropriate
    b. Correlation with other specimens, as appropriate
    c. Correlation with clinical information, as appropriate

Where no secondary Gleason grade exists, the primary Gleason grade is doubled to arrive at a Gleason score. The primary and secondary grades should be reported in parenthesis after the Gleason score, i.e. Gleason score 7 (3 + 4). If Gleason must be compressed for evaluation or reporting purposes, the groups should be 2–5, 6, 7, and 8–10, or 2–6, 7, and 8–10. Although Gleason scores range from 2 to 10, the grade seen at radical prostatectomy tends to be more restricted.

In radical prostatectomy specimens, where more than one separate tumor is identified, the Gleason scores of the individual tumors may be reported separately or at the very least the Gleason score of the most significant lesion should be recorded. For instance if there is a large Gleason score 5 transition zone cancer and a separate smaller Gleason score 7 peripheral zone cancer, both scores or at least the latter score should be reported rather than the scores being averaged.[19] Gleason scores may be grouped into differentiation or prognostic categories. Gleason score is emphasized as the grading system of choice and using the terms well differentiated, moderately differentiated, and poorly differentiated for grading is not recommended.[6]

Within radical prostatectomy specimens, as a result of the greater amount of tumor available for histological examination, a higher proportion of cases are found to contain more than two grades (i.e. tertiary Gleason pattern). There is no consensus about how to grade these tumors since the Gleason system only accounts for the primary and secondary patterns. The other controversy is how to grade tumors that are over 95% of one pattern, where there is only a very small percentage of higher-grade tumor. For example, if a tumor is composed of >95% Gleason pattern 3 and <5% pattern 4, some experts would assign a Gleason score 3 + 3 = 6, as it has been proposed that one needs over 5% of a pattern to be present for it to be incorporated within the Gleason score. Others might grade the tumor as Gleason score 3 + 4 = 7. In the only study to address this issue, it was found that the existence of a high-grade component, even if it constitutes less than 5% of the whole tumor, has a significant adverse influence on

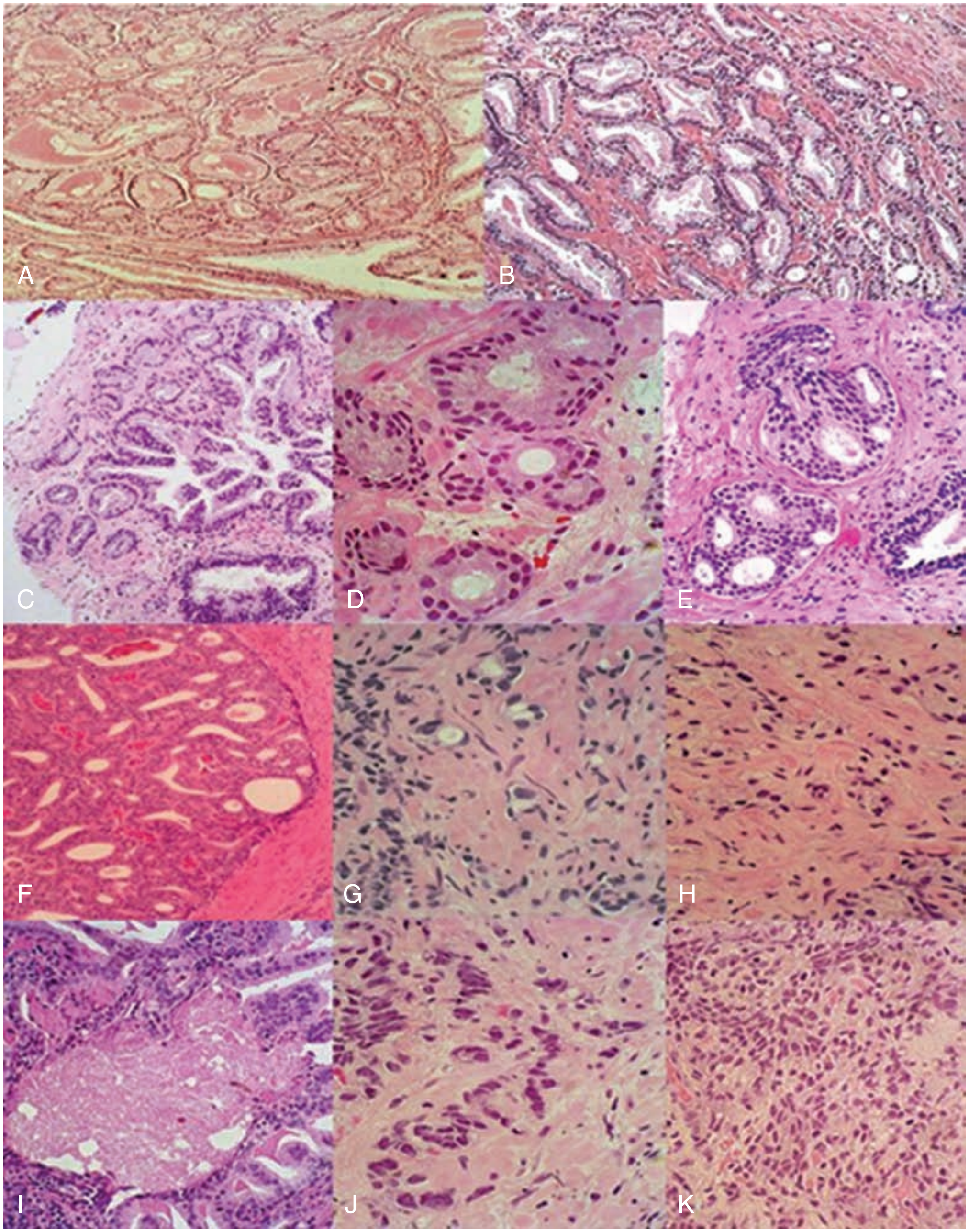

Figure 20.4 Examples of Gleason pattern 1 (A) and 2 (B), Gleason pattern 3 (C, D, E), Gleason pattern 4 (F, G, H), and Gleason pattern 5 (I, J, K). (Reproduced from Lopez-Beltran et al,[24] with permission.)

the overall biological behavior. The progression rate of Gleason scores 5–6 tumors with a tertiary component of Gleason pattern 4 is almost the same as that of a pure Gleason score 7 tumor. Gleason score 7 tumors with tertiary pattern 5 experience progression rates following radical prostatectomy approximating pure Gleason 8 tumors. On the other hand, no such significance could be seen in cases of Gleason score 8 with tertiary pattern 5, partly because of the limited sample size of men in this group, yet it is also likely that Gleason score 8 tumors are already bad so that the existence of pattern 5 elements makes no difference. As a consequence, two options were suggested to grade tumors containing tertiary high grades. One may grade the tumor strictly according to the original Gleason score but add a comment in the report noting the presence of the tertiary element.[25] The alternative is a 'modified' Gleason score, which is equal to primary grade plus worst grade. Others did not find a difference between cancers of Gleason score 6 with or without a small high-grade component.[24]

The group from Stanford has been a strong proponent of using the proportion of high-grade tumor (i.e. percent Gleason pattern 4/5) as the preferred method for grading prostate cancer. However, percent pattern 4/5 is only very predictive for progression at the extremes (greater than 70% or less than 20% pattern 4/5).[26] It has not been demonstrated that classifying tumors based on the percent pattern 4/5 is more predictive than stratifying patients into Gleason scores. Furthermore, assessing the percentage of Gleason pattern 4 is often difficult, as patterns 4 and 3 are often intimately admixed. Further difficulty in asking pathologists to derive a specific percentage of pattern 4/5 stems from studies demonstrating inter-observer variability in grading tumors with Gleason scores 5–7. Therefore, while accurate measurement of percentage of Gleason pattern 4 may not be practical, distinguishing Gleason score 3 + 4 from 4 + 3 is simpler, more reproducible, and more likely to be performed at routine pathological examination.[27]

When patients are under androgen blockade before surgery, the Gleason system cannot be applied. In such a situation, pathologists should indicate the degree of regression.[16]

Extent of local invasion

Extent of local invasion includes extraprostatic extension (Figure 20.5) and seminal vesicle involvement. Histologically, the prostatic capsule is not well defined. In some areas, there may appear to be a fibrous or fibromuscular band at the edge of the prostate, although in other areas normal prostatic glands extend out to the edge of the prostate without any appearance that there is a capsule. Because the prostate lacks a discrete capsule, the term 'extraprostatic extension' (EPE) has replaced 'capsular penetration' to describe tumor that has extended out of the prostate into periprostatic soft tissue.[2,28] Tumor abutting on or admixed with fat constitutes extraprostatic extension. EPE may also be reported when tumor involves perineural spaces in the neurovascular bundles, even in the absence of periprostatic fat involvement.

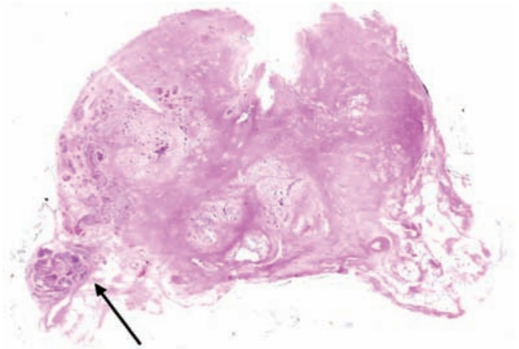

Figure 20.5 Whole-mount section showing prostate cancer located in the peripheral zone with extension to the extraprostatic tissues (i.e. EPE) (arrow).

The group from Baylor has been one of the few proponents of assigning levels to designate the extent of tumor going through the 'capsule'. As there is no well-defined prostatic capsule, it is hard to imagine how one would reproducibly diagnose tumor going into but not through the 'capsule.'

Difficulty in diagnosing EPE arises when tumor extends out of the prostatic gland and induces a dense desmoplastic response in the periprostatic adipose tissue. This is most commonly seen in prostatectomy specimens obtained after NHT. Because of the desmoplastic response, it can be difficult to judge whether the tumor has extended out of the gland or is within the fibrous tissue of the prostate. The best way of assessing whether EPE has occurred is to look at the adjacent edge of the prostate on scanning magnification where there is no tumor and follow the edge of the gland to the area in question to see whether the normal rounded contour of the gland has been altered by a protuberance corresponding to extension of tumor into the periprostatic tissue.

In certain locations, such as the anterior prostate and bladder neck regions, there is paucity of fat. In these locations EPE is determined when the tumor extends beyond the confines of the normal glandular prostate. At the apex, tumor admixed with skeletal muscle elements does not constitute EPE.[7]

The degree of EPE varies from only a few glands outside the prostate to cases with more extensive extraprostatic spread. The amount of EPE carries prognostic importance. Different ways have been used to define the amount of EPE. If it is equal to, or less than two high-power (40×) microscopic fields, then EPE is focal.[2] Any amount in excess of two high-power fields is considered to be either non-focal or extensive.

Staging

The protocol recommends the use of the TNM staging system for carcinoma of the prostate of the American Joint Committee on Cancer (AJCC) and the Union Internationale Contre le Cancer (UICC), as shown below.[29,30] The most recent revision was published in 2002. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathological classification is not possible. The prefix symbol 'p' refers to the pathological classification of the TNM (pTNM), as opposed to the clinical classification. Pathological classification is based on gross and microscopic examination (Table 20.3). By AJCC/UICC convention, the designation 'T' of the TNM classification refers exclusively to the first resection of a primary tumor. Therefore, pT entails a resection of the primary tumor or biopsy adequate to evaluate the highest pT category; pN entails removal of nodes adequate to validate lymph node metastasis; and pM implies microscopic examination of distant lesions.

Tumor remaining in a resection specimen following previous (neoadjuvant) treatment of

Table 20.3 Primary tumor, pathological (pT) (2002 revision)
(There is no pathological T1 category)

pT2: organ confined*
- T2a: tumor involves one-half of one lobe or less
- T2b: tumor involves more than half of one lobe, but not both lobes
- T2c: tumor involves both lobes

pT3: extraprostatic extension
- pT3a: extraprostatic extension
- pT3b: seminal vesicle extension

pT4: invasion of bladder **, rectum

*Invasion into the prostatic apex or into (but not beyond) the prostatic capsule is not classified as T3, but as T2. Tumor extension into periprostatic soft tissue, as opposed to organ-confined cancer (T2), is T3.
**See text.

any type (radiation therapy alone, chemotherapy therapy alone, or any combined modality treatment) is codified by the TNM, using a prescript ‘y’ to indicate the post-treatment status of the tumor (e.g. ypT2). The classification of residual disease may be a predictor of postoperative outcome. In addition, the ypTNM classification provides a standardized framework for the collection of data needed to accurately evaluate new neoadjuvant therapies.

Positive surgical margins

Patients with positive margins have a significantly increased risk of progression as compared to those with negative margins[31] (Figure 20.6). There are two causes for positive margins:

- Non-iatrogenic causes of positive margins: positive margins can result from a failure to widely excise EPE of tumor.
- Capsular incision: one cause of a positive resection margin is transection of intraprostatic tumor (capsular incision). These cases should be designated as pathological stage T2X, denoting that elsewhere the tumor is organ-confined, yet one cannot determine whether there is EPE in the region of capsular incision as the edge of the prostate has been left in the patient.

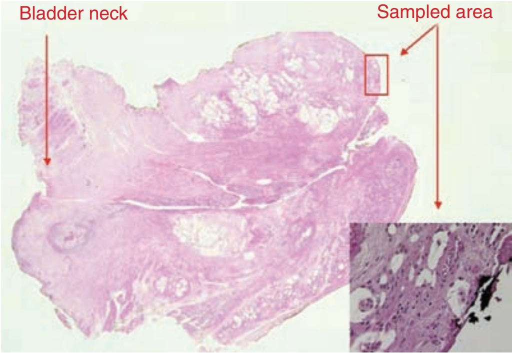

Figure 20.6 Whole-mount section of the prostate (lateral view) with cancer reaching the apical margin (the insert shows that cancer touches the inked margin).

Surgical margins should be designated as ‘negative’ if tumor is not present at the inked margin and as ‘positive’ if tumor cells touch the ink at the margin. Positive surgical margins should not be interpreted as EPE. If the surgical margin is positive, the pathologist should state this explicitly, although this finding is not relied upon for pathological staging. The examining pathologist should be aware of false-positive margins due to the penetration of ink into cracks present on the external surface. The main cause for discrepancy in the definition of a positive margin is seen in situations in which cancer was very close but not clearly touching the inked margin or when the color used to identify the margin appeared very pale.

The specific locations of the positive margins should be documented and there should be some indication (e.g. number of positive blocks, linear extent in millimeters) of the extent of margin positivity. The apex should be closely examined because of its unusual susceptibility to positive margins.[7,8,31]

There is no full consensus on the definition of the T category in the situation in which the prostate base/bladder neck is involved and the margin is positive. This problem is linked to the fact that the basal prostatic stroma blends imperceptively into the bladder neck musculature and, therefore, to the difficulty in defining the exact transition point from prostate base to bladder neck, even though the latter is composed of distinct large bundles of smooth muscle fibers.[9] Microscopic involvement of bladder neck muscle fibers in radical prostatectomy specimens should be defined as pT4.[32] Others[33] think that the microscopic involvement of bladder neck muscle fibers in radical prostatectomy specimens should not be equated with a pT4 designation, the latter generally requiring gross involvement of the bladder neck.

Tumor remaining in a patient after therapy with curative intent (e.g. surgical resection) is categorized by a system known as R classification.[26] This classification may be used by the surgeon to indicate the known or assumed status of the completeness of the surgical resection. For the pathologist, the R classification is relevant only to the margins of surgical resection specimens; patients with tumor involving the resection margins on pathological examination may be assumed to have residual tumor. Such patients may be classified as to whether the involvement is microscopic (R1) or macroscopic (R2).

Tumor that is locally recurrent after a documented disease-free interval following surgical resection is classified according to the TNM categories but modified with the prefix ‘r’ (e.g. rpT2).

The pathology report should also indicate the presence of normal prostate tissue at the resection margin level. This might help the urologist explain why the serum PSA in patients with such a feature remains detectable after radical prostatectomy. In fact, the serum PSA value, even though very low, is not linked to tumor recurrence and persistence but to incomplete resection of the prostate gland.

Volume of cancer

One of the most controversial aspects of the pathological assessment of radical prostatectomy specimens is the measurement of tumor volume. The critical and controversial question concerns whether tumor volume is an independent prognostic parameter once other routinely assessed variables are accounted for.

There is one situation where it is important to give some estimate of tumor volume at radical prostatectomy. As a consequence of screening for prostate cancer, we have seen an increase in the resection of prostates harboring cancers that are so small that they are histologically difficult to identify. These cases currently account for approximately 4% of our radical prostatectomy specimens. The pathologist has to specify in the pathology report that these tumors are ‘small’ or ‘minute’ (i.e. less than 0.5 cc) so that patients can be counseled that they are 100% cured of their tumor.

A consensus for a standard method of volume determination has not yet evolved. Volume is most precisely determined by stereological methods, using either planimetry or point counting based on overlaid grids. However, the time and labor involved in these approaches will probably not lead to their wide acceptance. It has been recommended that, at the very least, the proportion (percentage) of prostatic tissue involved by tumor be included for all specimens.[6]

Vascular invasion

By AJCC/UICC convention, vessel invasion (lymphatic or venous) does not affect the T category indicating local extent of tumor unless specifically included in the definition of a T category (Figure 20.7). In all other cases, lymphatic and venous invasions by tumor are coded separately. The TNM system uses the categories

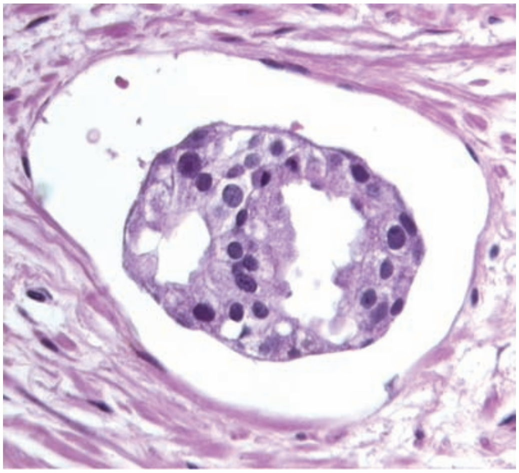

Figure 20.7 Vascular invasion (lymphatic).

L and V to indicate the presence of lymphatic or venous invasion. Most of the time when vascular invasion is noted, it is in tumors with fairly advanced pathology such that it is unclear as to its independent prognostic significance.[11,34]

Perineural invasion

Perineural invasion is one of the major mechanisms by which prostate cancer spreads out of the gland (Figure 20.8). Perineural invasion is almost ubiquitously present in radical prostatectomy specimens, such that it is not useful as a prognostic parameter and we do not record it within radical prostatectomy pathology reports. As with all of the other parameters, the key question is whether the presence of (intraprostatic) perineural invasion in the prostatectomy specimen is an independent prognosticator. At this time it is not entirely clear whether there are differences in terms of prognosis between intraprostatic and extraprostatic perineural invasion.[6,11]

Biomarkers to predict progression following radical prostatectomy

The drive to identify prognostic markers in prostate cancer is based on the perceived need to develop 'objective' markers to either supplant or supplement more 'subjective' markers that are currently in use (i.e. conventional histological grading). The more established biomarkers are as follows: DNA ploidy, microvessel density (angiogenesis), KI-67, neuroendocrine differentiation, p53, $P27^{kip1}$, $p21^{WAF1}$, bcl-2, Her-2/neu, E-cadherin, CD44, retinoblastoma (Rb) proteins, apoptotic index, androgen receptor status, PSA and PSAP expression, and nuclear morphometry.[6] These newer markers (and techniques) must be approached critically and rationally to determine whether they provide additional prognostic information beyond that which is currently available using more conventional parameters.[2,7]

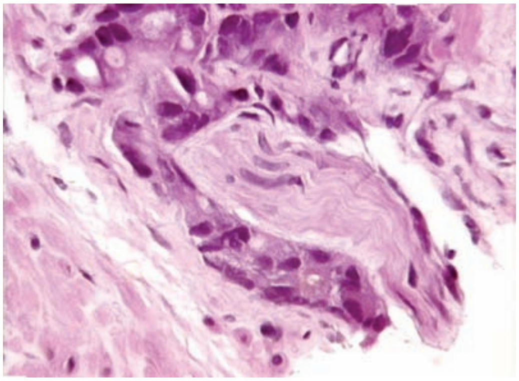

Figure 20.8 Perineural invasion.

PELVIC LYMPH NODE ASSESSMENT

The adverse prognosis of metastatic disease to the pelvic lymph nodes is universally accepted. The incidence of pelvic lymph node metastases at the time of radical prostatectomy has decreased over the last couple of decades.[3,7,35] As a consequence of the declining incidence, concerns have been raised as to whether pelvic lymphadenectomy is necessary in all patients, especially those with a low risk of having positive lymph nodes based on preoperative clinicopathologic findings. The major factors contributing to this decrease are better patient selection as to who is a good candidate for surgery and the earlier detection of prostate cancer, both resulting from the use of serum PSA testing.

Intraoperative pathological assessment

The handling of lymphadenectomy specimens at the time of surgery is controversial and depends on the philosophy of the urologist. Some urologists will abort the radical prostatectomy in cases with positive lymph nodes identified at the time of surgery, since surgery will not be curative. With these urologists, the pathologist should try to optimize the identification of metastatic disease at the time of frozen section. Other urologists will proceed with radical prostatectomy when positive lymph nodes are found intraoperatively, as long as patients are projected to have a long survival and might benefit in terms of local control.

It is not practical to freeze all of the pelvic lymph nodes, especially given the low likelihood of finding metastatic disease even on permanent sections. A more reasonable approach would be to preoperatively identify clinical parameters associated with such a low risk of lymph node metastases that frozen sections need not be performed.[16]

Routine processing of pelvic node specimen

In 6.5% of the cases the only lymph node metastasis is not in a grossly recognized lymph node but in small lymph nodes embedded in the adipose tissue. Based on this, all of the adipose tissue from the pelvic lymphadenectomy specimens should be submitted for histological examination. The detection of pelvic lymph node metastases may be enhanced through the use of special techniques. In particular, micrometastases can be immunohistochemically detected using antibodies to a keratin cocktail.

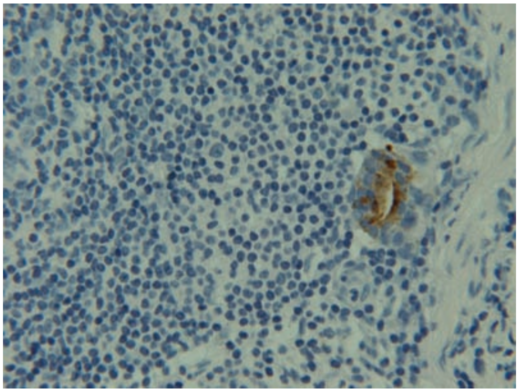

Figure 20.9 Isolated tumor cells in a lymph node found by immunohistochemical examination with an antibody directed against PSA (prostate-specific antigen).

Isolated tumor cells

Isolated tumor cells (ITC) are single cells or small clusters of cells not more than 0.2 mm in greatest dimension. Lymph nodes or distant sites with ITC found by either histological (immunohistochemical) examination (Figure 20.9) or non-morphological techniques (e.g. flow cytometry, DNA analysis, polymerase chain reaction [PCR] amplification of a specific tumor marker) should be classified as N0 or M0, respectively. Specific denotation of the assigned N category is suggested for cases in which ITC are the only evidence of possible metastatic disease[36] (Table 20.4).

CONCLUSIONS

Substantial effort has been expended in recent years in describing the available factors and

Table 20.4 Regional lymph modes (pN0) and isolated tumor cells

- pN0: no regional lymph node metastasis histologically, no examination for isolated tumor cells (ITC)
- pN0(i–): no regional lymph node metastasis histologically, negative morphological (immunohistochemical) findings for ITC
- pN0(i+): no regional lymph node metastasis histologically, positive morphological (immunohistochemical) findings for ITC
- pN0(mol–): no regional lymph node metastasis histologically, negative non-morphological (molecular) findings for ITC
- pN0(mol+): no regional lymph node metastasis histologically, positive non-morphological (molecular) findingsfor ITC

determining their predictive value for staging, cancer recurrence, and patient survival. Pathologists derive many clinically important predictive factors in prostate cancer from light microscopic examination of RP specimens. The goal is to tailor the therapeutic approach to the clinical, morphological, and molecular features of each patient. Although in the future conventional histology will not be replaced in the evaluation of prostate cancer at radical prostatectomy and its correlation with outcome, it will undoubtedly be augmented by new markers and modern techniques.[10,37]

Practice points

- The whole prostate was fixed in 10% neutral buffered formalin for 24 hours. The volume of fixative should exceed 5–10 times the prostate itself and the prostate should not touch the sides of the container.
- The entire external surface of the prostate should be carefully inked either by immersion into India ink or by painting the surface with different colors of ink to ensure the proper orientation.
- The seminal vesicles are amputated at the base and then cut longitudinally with a sandwich technique.
- The apex and bladder base parts are removed by a transversal section performed at 4 mm from the distal and proximal margins of the prostate, perpendicular to the rectal surface. Then, both margin specimens were cut parasagittally at 3 mm intervals perpendicular to the inked surface and all margin tissue was submitted for histological examination.
- The remaining prostate specimen was serially sectioned transversely at 3 mm intervals perpendicular to the rectal surface.
- When using the partial sampling method, the remaining prostatic slices should be well preserved in the original orientation for the occasional requirements of additional sections.
- If no cancer is identified on the submitted sections or the tumor closely approaches the surgical margin, pathologists should embed all other slices for histological examination.
- When tumor is not readily identified on the slides, even after submission of the entire prostate, one should cut deep sections from all available blocks.
- The pathology report has to contain prognostically useful data derived from the evaluation of the RP specimen.
- Submit all of the pelvic lymphadenectomy specimens routinely for histological examination to avoid the occasional misdiagnoses in examining the grossly identified lymph nodes only.

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CHAPTER 21

Rehabilitation of sexual function

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INTRODUCTION

Radical prostatectomy is an increasingly used therapeutic option for patients with clinically localized prostate cancer and a life expectancy of at least 10 years.[1] The pioneering work by Walsh and Donker[2] significantly contributed to the understanding of the surgical anatomy of the prostate and posed the bases for the subsequent development of the anatomical radical prostatectomy technique: i.e. a surgical approach aimed at completely excising the prostate, providing optimal cancer control while maintaining the integrity of the anatomical structures devoted to the functions of urinary continence and sexual potency.[3–5] Since the initial reports on this technique, an increasing number of studies have reported very satisfactory postoperative rates of urinary continence while the preservation of erectile function after surgery has been clearly shown to be a major challenge for most urologists.[6–8] This finding has contributed to the development of an increasing interest in the elucidation of the pathophysiology of postoperative erectile dysfunction (ED) and its potential prophylaxis and treatment.[9,10] Furthermore, ED after radical prostatectomy shows a profound effect on quality of life (QoL). Indeed, it has been shown that more than 70% of patients who had undergone radical retropubic prostatectomy had a moderately or severely affected QoL because of their postoperative ED, when investigated.[11] Moreover, although the International Index of Erectile Function (IIEF)[12] has been widely accepted as a validated instrument to assess ED, it has been demonstrated that different definitions of potency after surgery yield different results when applied to the same patients at the same time. This underlines the observation that sexual function entails more than penile erection firm enough for intercourse, as the classic definition of potency, in fact demonstrated variable agreement.[13]

PATIENT SELECTION

The anatomical nerve-sparing approach to the prostate is considered for patients with clinically localized prostate cancer. Clinical stages T1 and T2 patients, as defined following digital rectal examination and/or transrectal ultrasonography of the prostate, are the best candidates. As clinical stage is often correlated with both prostate-specific antigen (PSA) values and the biopsy Gleason score, it has been suggested that a nerve-sparing approach may be considered in patients with PSA <10 ng/ml and a Gleason score ≤7.[14]

Patients being considered for a nerve-sparing radical prostatectomy (NSRP) should be potent prior to the procedure. This is of major importance, as patients who report some degree of erectile dysfunction or patients who use phosphodiesterase type 5 inhibitors (PDE5-I) prior to the procedure are more likely to develop severe erectile dysfunction after the procedure itself.[15] The use of validated questionnaires such as the IIEF[12] may facilitate the diagnosis of preoperative erectile dysfunction during the initial patient assessment. This questionnaire assesses various domains of male sexuality, including erectile and ejaculatory function, orgasm, desire, and intercourse satisfaction and, by reviewing the results of this patient self-assessment, interesting baseline information is always obtained. Morphology of the corpora cavernosa deteriorates with aging and this may be correlated with the high prevalence of erectile dysfunction seen in aging men.[16] Rates of recovery of erectile function after a nerve-sparing radical prostatectomy are inversely correlated with the patient's age: i.e. best postoperative potency rates are obtained in the younger patient population and it seems reasonable to consider patients ≤65 years of age as candidates for a nerve-sparing procedure.[3,17] Patient age also seems to be one of the most important factors for the recovery of sexual potency after unilateral nerve-sparing surgery. Indeed, in a group of 46 patients who received unilateral nerve-sparing radical retropubic prostatectomy, 14 (30.4%) regained fully potency after surgery and, in the vast majority of them, recovery occurred within a period of 18 months. Of these patients, those aged <60 years old reported the highest rate of recovery of potency sufficient for vaginal penetration after a mean of 13 months after surgery.[18] Comorbid conditions seem also to affect the recovery of spontaneous erections postoperatively, as they may impact on the baseline penile hemodynamics. Namely, a concomitant diagnosis of diabetes mellitus, hypertension, ischemic heart disease, or hypercholesterolemia, or a history of cigarette smoking identified at the time of the preoperative patient assessment should be taken into account as a potential negative predictive factor for potency recovery after surgery.[15] Although a higher prostate volume could be associated with higher intraoperative bleeding, it does not seem to influence postoperative potency rate.[19,20] Nevertheless, body weight does not seem to be related to the feasibility of a nerve-sparing approach, also in clinically obese patients.[20]

SURGICAL TECHNIQUE

In suitable candidates, radical excision of the prostate should be performed with the objective of achieving total cancer control: i.e. removing all cancer present in the prostatic tissue, while maintaining the integrity of the anatomical structures on which urinary continence and erectile function are based. Namely, the corpora cavernosa receive the innervation responsible for erections through the cavernosal nerves, which branch out from the pelvic plexus. This latter structure is located adjacent to the tip of the seminal vesicles on the anterolateral wall of the rectum and may be damaged during radical prostatectomy. The cavernous nerves course adjacent to small vessels forming the so-called neurovascular bundle along the posterolateral margin of the prostate, bilaterally, and are located between the visceral layer of the endopelvic fascia and the prostatic fascia. The neurovascular bundle is located at the 5 and 7 o'clock positions at the level of the membranous urethra and, after piercing the urogenital diaphragm, it enters the corpora cavernosa, where it innervates the smooth muscle cells of the penile vessel walls and sinusoids.[21] It has been suggested that while the main trunk of the cavernous nerves runs posterolateral to the prostate from the level of the seminal vesicles to the prostatic apex,[22] a significant amount of nerves branch off the pelvic plexus to course along the anterolateral surface of the prostate.[23] These nerves run between the prostatic and the levator fascia.[21,23–25] Distally, fibers of the cavernous nerves join together at the level of the urethral sphincter and are mainly located from the 4 to 5 o'clock positions and from the 7 to 8 o'clock positions. Based on a better understanding of the surgical anatomy of the prostate, Walsh and Garcia have clearly described the technique of anatomical radical prostatectomy in a step-by-step fashion.[24] The use of a frontal xenon light and of magnifying loupes significantly improves vision during the procedure and the authors of this review feel that this armamentarium should always be used when performing nerve-sparing radical prostatectomies. Indeed, it has been recently demonstrated how use of 2.5× optical loupe magnification during neurovascular bundle preservation was associated with a better recovery of erectile function after surgery in a follow-up of more than 1 year.[26] Some crucial surgical steps deserve particular attention. Following pelvic lymphadenectomy, the endopelvic fascia is incised to allow the dissection of the prostatic apex. Care should be taken to ligate small branches of pudendal vessels, which are located just underneath the endopelvic fascia in the area of the prostatic apex; cautery should not be used to secure these vessels, in order to avoid damage to pudendal nerve branches that are also located there. Ligation of the Santorini's plexus is a fundamental step in the procedure, as it must guarantee perfect hemostasis in order to obtain the best visualization of the surgical field during the excision of the prostate. Walsh has suggested to ligate the Santorini's plexus distally first and to subsequently divide it with scissors; control of the proximal stump of the venous plexus is then achieved with a V-shaped suture, which avoids a central retraction of the neurovascular bundles and thus facilitates the nerve-sparing procedure. It has been recently suggested that control of Santorini's plexus might be performed by using a small Allis clamp to grasp the two medial borders of the incised levator fascia.[27] This maneuver is used to pull together only the superficial components of the Santorini's plexus; then, a 3-0 Monocryl (poliglecaprone) suture on a UR-6 needle is passed distal to the Allis clamp. It is important to note that this suture is not used to control all branches of the Santorini's plexus, as it is passed quite superficially to avoid any damage to the urethral sphincter. Indeed, it allows for approaching the external urethral sphincter under direct vision, thus limiting the damage possibly occurring during its dissection. This passage is repeated twice and the suture is tied while leaving the Allis clamp in place. This maneuver allows the branches of the Santorini's plexus to be pulled together and facilitates its subsequent division. The Santorini's plexus is then sharply divided. A running suture with a 3-0 Monocryl on a UR-6 needle is used to control bleeding from the deeper portion of the distal trunk of the Santorini's plexus. This suture must take only the Santorini's plexus; neither the urethral sphincter nor the most distal fibers of the levator ani (also named levator urethrae) should be included in this suture, thus leaving the external sphincter and levator ani muscles completely intact. Once these bleeders are controlled, a running suture controlling the proximal (prostatic) trunk of the Santorini's plexus is used following the technique described by Walsh.[2,3] After controlling and dividing the Santorini's plexus, the visceral layer of the endopelvic fascia should be bluntly incised on the lateral side of the prostate to allow for the gentle lateral displacement of the neurovascular bundles, which is obtained with the use of small sponge sticks. If this maneuver is performed correctly, the neurovascular bundles become clearly visible along their entire course from the membranous urethra and the seminal vesicles in most patients. Other investigators subsequently proposed different techniques aimed at achieving the best possible rates of postoperative normal urinary continence and potency. Namely, the importance of removing the prostate while leaving in place a large portion of the levator and prostatic fasciae that cover the gland has been recently proposed, by using both open and robotic techniques.[23,28] A novel nerve-sparing surgical approach has been recently proposed that consists of a high anterior incision of the levator and prostatic fasciae aimed at preserving efficiently the urethral sphincter and neurovascular bundles during open radical retropubic prostatectomy. Starting from the bladder neck, using dissecting scissors, the levator and prostatic fasciae are perforated and the development of the plane running between the prostatic capsule and the prostatic fascia is initiated. This plane is developed in a step-by-step fashion, from the region of the bladder neck to the urethral sphincter. The correct plane is easily identified, as the reflection of the prostatic fascia is smooth and veins can be seen clearly, as through a transparent sheet. This maneuver must be performed very gently. In this way, we detach the prostatic fascia from the prostatic capsule and from the urethral sphincter. This maneuver allows for preservation of all vessels and nerves included between the prostatic and levator fasciae. The space created on both sides between the lateral border of the urethral sphincter, the prostatic apex, and the reflected prostatic fascia is usually remarkable in size. The dissection of the anterolateral surface of the prostate is extended as laterally as possible. When this dissection is completed on both sides of the prostate, the urethral sphincter and the prostatic apex are clearly visible.

By performing an incision of the levator fascia at the 1 and 11 o'clock positions to start the dissection of the neurovascular bundle, the largest possible fraction of the pelvic plexus branches, including cavernous nerve fibers, may be preserved.

Early release of neurovascular bundles laterally, starting from the apex of the prostate just following the division of anterior urethra, has also been proposed and associated with a greater percentage of patients reporting preserved erectile function after surgery, if compared with a standard release of neurovascular bundles' technique.[26]

It is mandatory to avoid the use of cautery during every step of the prostatic excision. Recently, the Johns Hopkins group has also suggested that any type of energy used during the dissection of the prostate is going to inevitably damage the neurovascular bundles: ultra-fine clips and suture ligatures are thus recommended to guarantee adequate hemostasis during an NSRP.[29] As the pelvic plexus is located adjacent to the posterolateral tips of the seminal vesicles, particular care should be taken while excising them. The possible advantage of partially excising the seminal vesicles to reduce the risk of damaging the pelvic plexus, and thus affecting postoperative urinary continence and erectile function, has been reported.[30] When pelvic hematomas occur, it is advisable to drain them surgically, as the fibrosis occurring after the slow spontaneous resolution of any blood collection significantly lengthens the duration of cavernosal neuropraxia. Although the number of cases performed per unit of time (surgeon's volume) is a recognized predicting factor for success/failure to maintain potency following an NSRP, it has now been suggested that the surgeon himself is probably playing the most fundamental role in determining the patient's postoperative outcome: in other words, a large-volume surgeon may potentially keep doing things wrong if his surgical technique is not adequate.[31] An important take-home message is thus the need to compare one's own surgical technique with that used by recognized experts in this field. Reviewing the videotapes of one's own nerve-sparing radical prostatectomies and comparing the surgical technique with the results seen in terms of margins status, urinary continence, and erectile function may be of significant importance, as it allows the surgeon to identify the parts of the operation at higher risk for surgical errors.[32]

PATHOPHYSIOLOGY OF ERECTILE DYSFUNCTION FOLLOWING NERVE-SPARING RADICAL PROSTATECTOMY

Patients undergoing NSRP often experience impairment of erections in the early postoperative period. This has been related to the development of neuropraxia, which is believed to be caused by some damage to the cavernosal nerves that inevitably occurs during the excision of the prostate, even in the hands of most experienced surgeons. Absence of early postoperative erections is associated with poor corporeal oxygenation, which may facilitate the development of corporeal fibrosis, ultimately leading to veno-occlusive dysfunction.[33] Recently, the role of apoptosis has been considered in the pathophysiology of post-prostatectomy ED. Apoptosis, or programmed cell death, is essential for the normal development of multicellular organisms as well as for physiological cell turnover. Morphologically, this phenomenon is characterized by chromatin condensation, membrane blabbing, and cell volume loss. In the penis, chronic hypoxia and denervation have been shown to stimulate apoptosis: it is possible that cellular apoptosis leads to increased deposition of connective tissue that may finally lead to a decrease in penile distensibility.[34–37] Recently, User et al[38] have elegantly elucidated the role of apoptosis in the pathophysiology of post-prostatectomy erectile dysfunction in the rat model. Postpubertal rats were randomized to bilateral or unilateral cavernous nerve transection vs a sham operation. At different time intervals following the procedure, penile wet weight, DNA content, and protein content were measured. Tissue sections of the penis were stained for apoptosis and the apoptotic index was calculated. Finally, staining for endothelial and smooth muscle cells was done to identify the apoptotic cell line. Wet weight of the denervated penes was significantly decreased after bilateral cavernous neurotomy, whereas unilateral cavernous neurotomy allowed much greater preservation of penile weight. DNA content was also significantly reduced in bilaterally denervated penes, whereas no difference was found between unilaterally denervated penes and controls. Bilateral cavernous neurotomy induced significant apoptosis, which peaked on postoperative day 2. In addition, it was found that most apoptotic cells were located just beneath the tunica albuginea of the corpus cavernosum, i.e. the anatomical area where the subtunical venular plexus is located. Finally, the authors found that apoptotic cells were smooth muscle cells and not endothelial cells. The subsequent hypothesis suggested by the authors was that the bilateral injury to the cavernous nerves may induce significant apoptosis of smooth muscle cells, particularly in the subtunical area, thus causing an abnormality of the veno-occlusive mechanism of the corpus cavernosum. Apoptosis seems to play a role also in the genesis of ED seen in the aging population (which is clearly of crucial importance in the radical prostatectomy patient group) as it has been shown that antiapoptotic genes and proteins are expressed in young rats but not in aging rats.[34] These findings on apoptosis following radical prostatectomy confirm that most patients reporting postoperative ED develop massive corporeal venous leaks in the long term.[39] However, a reduction of the arterial inflow to the corpora cavernosa in patients with post-prostatectomy erectile dysfunction has been reported by several authors as a significant etiological cofactor.[40,41] Postoperative penile hypoxia seems to play an important role in inducing histological, and thus functional, changes of the corpora cavernosa after surgery. Indeed, a recent clinical trial performed by Iacono et al has clearly demonstrated how in a selected preoperatively potent population of 19 non-diabetic patients undergoing radical prostatectomy and penile biopsies both before, 2, and 12 months after surgery, a progressive increase in penile organized collagen content and a decrease in interstitial elastic fibers and smooth muscle cells were evident after surgery.[42]

The more relevant structural penile modifications were reported at the 12-month follow-up biopsy evaluation. Interestingly, none of the preoperatively potent patients enrolled either experienced spontaneous erections or responded to prophylactic postoperative sildenafil administration (100 mg, once weekly for 3 weeks, starting 2 months after surgery), thus strongly suggesting that a non-nerve-sparing procedure had been performed in the same patients. In conclusion, the postoperative combination of reduced penile arterial inflow and excessive venous outflow due to the apoptosis-induced damage of the veno-occlusive mechanism lead to reduced oxygen transport and increased production of transforming growth factor-beta. This subsequently causes significant tissue damage – i.e. increased corporeal fibrosis – which is not only at the root of the known penile hemodynamic abnormality but also probably causes the postoperative decrease of penile length recently reported in an interesting study.[43]

PHARMACOLOGICAL PROPHYLAXIS AND TREATMENT OF POSTOPERATIVE ERECTILE DYSFUNCTION

Prophylaxis

A better understanding of the pathophysiology of post-prostatectomy ED, including the concept of tissutal damage induced by poor corporeal oxygenation, has paved the way for the application of pharmacological regimens aimed at improving early postoperative corporeal blood filling. Montorsi et al[44] showed that, by using intracorporeal injections of alprostadil early after a bilateral NSRP, the rate of recovery of spontaneous erections was significantly higher than observation alone. In the authors' experience, alprostadil injection therapy should be started as soon as possible after the procedure, usually at the end of the first postoperative month. The initial dose of alprostadil is 5 µg. Patients should be instructed to use injections 2 or 3 times per week in order to obtain penile tumescence; injections are not necessarily associated with sexual intercourse but it is clear that, if the patient desires, he may be able to resume satisfactory sexual intercourse with penetration as soon as he is able to identify the correct dosing of the drug.

Brock et al[45] have also shown that the continuous use of intracavernous alprostadil injection therapy was able to significantly improve penile hemodynamics and return of spontaneous erections (either partial or total) in patients with arteriogenic ED, thus confirming a potential curative role of this therapeutic modality in selected patients. These data have also been recently confirmed by Mulhall et al,[46] who showed that the prophylactic use of intracorporeal injections of alprostadil in patients non-responding to oral sildenafil resulted in higher rates of spontaneous functional erections and erectogenic drug response 18 months after NSRRP. The early postoperative use of intracavernosal injection therapy may also exert a significant psychological role. Commonly after an NSRP, with the slow return of spontaneous erections, a dysfunctional sexual dynamic may develop in couples. The patient withdraws sexually as he is increasingly discouraged with his lack of erectile function, which is a constant reminder of his cancer. The female partner, relieved that the patient has survived the surgery, may be satisfied with his companionship and is not anxious to upset him by making sexual overtures that may frustrate him. Successful intracorporeal injection therapy early after radical prostatectomy may contribute to break this negative cycle.[15]

Prophylactic administration of a vacuum constriction device (VCD) has also been recently proposed as an early penile rehabilitation approach aimed to promote an adequate cavernosal oxygenation and therefore to prevent penile fibrosis after surgery.[47]

The advent of PDE5-I in the treatment of ED has clearly revolutionized the management of this medical condition. This class of agents acts within the smooth muscle cell by inhibiting the enzyme phosphodiesterase type 5 which naturally degrades cyclic guanosine monophosphate (cGMP), an intracellular nucleotide that acts as second messenger in the process of smooth muscle cell relaxation. The cascade of intracellular events, which leads to the relaxation of the smooth muscle cell, is initiated by the release of nitric oxide following sexual stimulation. Both intracorporeal cavernous nerve terminals and endothelium release nitric oxide, which as a gas diffuses into the smooth muscle cells and activates the enzyme guanylate cyclase, which ultimately catalyzes the conversion of guanosine triphosphate to cGMP. Increased levels of cGMP lead to the activation of cGMP-specific protein kinases, which activate further intracellular events, leading to the final reduction of intracellular calcium – this being associated with smooth muscle cell relaxation. At present, sildenafil, tadalafil, and vardenafil are approved for clinical use in the European Union and have also been utilized to treat post-prostatectomy ED.

The rationale for the use of these drugs as prophylaxis is not completely understood yet. However, recent studies have elucidated some mechanisms potentially involved.[48–52] The basic concept would be to administer a PDE5-I at bedtime in order to facilitate the occurrence of nocturnal erections, which are believed to have a natural protective role on the baseline function of the corpora cavernosa. Montorsi et al showed that when sildenafil 100 mg is administered at bedtime in patients with ED of various etiologies, the overall quality of nocturnal erections, as recorded with the RigiScan device, is significantly better than those obtained after the administration of placebo.[48] Furthermore, experimental data regarding the potential mechanisms involved in chronic administration of sildenafil have been very recently published.[49] Indeed, the effect of an 8-week-long treatment with sildenafil (60 mg/kg/day subcutaneously) in male rats was evaluated on electrically induced erectile responses in vivo before and after an acute injection of sildenafil (0.3 mg/kg intravenously). Furthermore, endothelial-dependent and -independent relaxations of strips of corpus cavernosum were examined in vitro and compared with cavernosal strips of untreated rats. Interestingly, the authors found that endothelial relaxation induced by acetylcholine was significantly enhanced in rats treated chronically with sildenafil compared with untreated rats. This could imply that either muscarinic receptors or the transduction mechanisms leading to the activation of endothelial nitric oxide synthase are up-regulated by a chronic sildenafil treatment. Moreover, functional in-vivo evaluations showed that chronic administration of sildenafil significantly enhanced frequency-dependent erectile response and was associated with a greater response to an acute injection of sildenafil in treated rats compared with controls. This study represents the first experimental support for chronic consumption of sildenafil, which could be associated with a higher rate of erectile function recovery after radical prostatectomy.

In this context, Padma-Nathan et al[50] recently reported on the prospective administration of sildenafil 50 and 100 mg vs placebo, daily and at bedtime, in patients undergoing bilateral nerve-sparing radical prostatectomy who were potent preoperatively. Four weeks after surgery, patients were randomized to sildenafil or placebo, which were carried on for 36 weeks. Eight weeks after discontinuation of treatment, erectile function was assessed with the question 'Over the past 4 weeks, have your erections been good enough for satisfactory sexual activity?' and by IIEF and nocturnal penile tumescence (NPT) assessments. Responders were defined as those having a combined score of ≥8 for IIEF questions 3 and 4 and a positive response to the above question.

Twenty-seven percent of the patients receiving sildenafil were responders, i.e. demonstrated return of spontaneous normal erectile function, compared with 4% in the placebo group ($p = 0.0156$). Postoperative NPT assessments were supportive. We believe that in the hands of experienced surgeons a 27% overall rate of return to normal erectile function after a bilateral nerve-sparing procedure is far from being impressive, but the important message from this study is that daily bedtime administration of sildenafil 50 or 100 mg after this procedure should be able to improve every surgeon's baseline results. Although similar data are not available yet for tadalafil and vardenafil, we believe there is no reason not to expect similar findings with these drugs.

Moreover, the rationale for PDE5-I administration at bedtime in patients undergoing non-sparing radical retropubic prostatectomy (NSRRP) has recently been evaluated by Bannowsky et al.[51] In fact, in a cohort of 27 patients submitted to NSRRP, nocturnal penile tumescence and rigidity (NPTR) recording during the acute phase after surgery showed residual erectile function as early as the first night after catheter removal. Conversely, in a small control group of four patients treated with non-NSRRP, no nocturnal erections were recorded early after catheter removal. Based on these results, the authors concluded that in cases of early nocturnal tumescence, application of a PDE5-I can support successive organ rehabilitation. However, further studies are needed to confirm the rationale of this approach.

Furthermore, early use of high doses of sildenafil after radical prostatectomy seems to be associated with preservation of smooth muscle content within human corpora cavernosa. Indeed, Schwartz et al enrolled 40 potent patients affected by localized prostate cancer who underwent radical retropubic prostatectomy at a single institution and were subsequently treated either with daily sildenafil 50 mg (group 1) or 100 mg (group 2) for 6 months starting from the day of catheter removal.[52] Patients underwent percutaneous penile biopsy both preoperatively (under general anesthesia prior to surgical incision) and 6 months after surgery (using local anesthesia). Interestingly, while in group 1 there was no statistically significant change in the mean intracavernosal smooth muscle content between the preoperative and postoperative measurements (51.1% and 52.6%, respectively), in group 2 a statistically significant increase in mean smooth muscle content after surgery (42.8% vs 56.8%, $p < 0.05$) has been found. Thus, although it remains unclear how the chronic administration of sildenafil could increase the intracavernosal smooth muscle content after surgery, daily high-dose administration of PDE5-I may be a key factor in the cavernosal smooth muscle preservation, thus reinforcing the idea of the clinical application of sexual pharmacological prophylaxis after surgery.

However, despite the enthusiasm associated with these studies, the benefit induced by a rehabilitative PDE5-I approach compared with an on-demand PDE5-I administration schedule has not been confirmed. We recently prospectively studied a cohort of 80 patients submitted to bilateral nerve-sparing radical retropubic prostatectomy (BNSRRP) with adequate postoperative erectile function data 12 months after surgery.[53] Patients were not-randomly assigned to four different groups after BNSRRP: no erectile therapy; intracavernosal injection of prostaglandin E_1 on demand; PDE5-I on demand; and rehabilitative PDE5-I therapy (either every day or every other day for 3 months). Interestingly, we did not record any significant difference in the mean IIEF-erectile function domain score between patients who received PDE5-I on demand and those treated with a rehabilitative intent 12 months after surgery. However, further large randomized trials are needed to confirm the validity of these preliminary data.

Therefore, an open debate regarding the efficacy of oral rehabilitation after radical prostatectomy is still ongoing.

Recently, a prophylactic regimen with methylprednisolone has been used in an interesting trial involving 70 preoperatively young patients (40–60 years old) undergoing BNSRRP who were randomized to receive either 6 days of placebo or escalating doses of methylprednisolone starting from postoperative day 1.[54] The rationale of steroid use early after surgery was based on the potential use of this treatment in reducing the surgical neural inflammation and local edema that might contribute to dysfunction of neurovascular bundles after surgery. Nevertheless, no clinical benefit has been reported in patients receiving steroids compared with the placebo group in terms of erectile function recovery based on IIEF evaluation at 3-, 6-, and 12-month evaluation ($p = 0.08$, $p = 0.50$, $p = 0.71$, respectively). Even in the presence of disappointing results, many important factors, such as timing of administration of the drug, doses used, and duration of therapy, might be considered to be potential explanations for lack of steroid-induced benefits.

In practical terms, we feel that the need for postoperative prophylactic therapy should be discussed with the patient when counseling him about radical prostatectomy as one of the treatment options for prostate cancer. Patients must have the chance to guide their choice also by being informed on the pharmacological approaches needed to recover a normal postoperative erectile function.

Treatment

Phosphodiesterase type 5 inhibitors

PDE5-I have acquired an established role in the treatment of post-prostatectomy erectile dysfunction. As the mechanism of action of this class of drugs implies the presence of nitric oxide within the corporeal smooth muscle cells, only patients undergoing a nerve-sparing procedure should be expected to respond to these agents. Sildenafil is the drug which has been studied more extensively in this patient subgroup, as it has been on the market worldwide since 1998. In general terms, it is now known that sildenafil gives the best results in young patients: the <60-year-old age group being the best responding, in patients treated with a bilateral nerve-sparing procedure, and in patients who show some degree of spontaneous postoperative erectile function. Sildenafil is usually administered at the largest-available dose, although it is common experience to have post-prostatectomy patients responding also to the 25 and 50 mg doses. Typically, the response to sildenafil has been shown to improve as time passes by after the procedure: best results are seen from 12 to 24 months postoperatively.[5,55–62] Unfortunately, no data coming from multicenter, randomized, placebo-controlled trials assessing sildenafil in patients undergoing nerve-sparing radical prostatectomy are available to date. It has been suggested that the early postoperative prophylactic administration of alprostadil injections allowed a subsequent better response rate to sildenafil to be obtained with lower doses of the drug being necessary.[63] Several studies have been published regarding the postoperative role of sildenafil to be obtained as treatment of ED after a nerve-sparing procedure.[55–59] The response rate to sildenafil treatment for ED after radical prostatectomy (RP) ranged from 35% to 75% among those who underwent nerve-sparing surgery and from 0% to 15% among those who underwent non-nerve-sparing surgery. A recent report has identified many factors significantly associated with a successful outcome of sildenafil treatment after surgery in terms of erectile response, including the presence of at least one neurovascular bundle, a preoperative good erectile function (Sexual Health Inventory of Men [SHIM] score ≥15), age ≤65 years old, and interval from radical prostatectomy to drug use (more than 6 months).[61]

Zagaja et al[58] found an inverse relationship between age and response to sildenafil therapy for ED post-RP. Among men who underwent bilateral nerve-sparing (BNS) surgery, response rates decreased from 80% in those <55 years old, to 45% in those aged 56–65 years old, and to 33% in those >66 years old. Zippe et al stratified response rate by three time intervals post-RP and by sildenafil dosage. The response rate increased with time during the first year – 3–6 months (44%), 6–12 months (55%), and >12 months (53%) – and more responders required the 100 mg dose of sildenafil (71%) than the 50 mg dose (29%). Thus, the data suggest that the early initiation of treatment is recommended, but realistic improvement in response should not be expected until 1 year after surgery.[56] Raina et al recently reported the long-term results of sildenafil use in patients affected by ED after radical prostatectomy.[64] This study enrolled 91 patients stratified according to the type of nerve-sparing procedure they had undergone: bilateral nerve-sparing ($n = 53$), unilateral nerve-sparing ($n = 12$), and non-nerve-sparing ($n = 26$) radical retropubic prostatectomy. All patients, at least 3 months after surgery, were prescribed sildenafil with the starting dose of 50 mg, which was tritated up to 100 mg in case of not-satisfactory response. At the 12-month assessment performed by means of SHIM and Erectile Dysfunction Inventory for Treatment Satisfaction (EDITS) questionnaire filling, 48 out of the 91 patients enrolled (52.7%) reported having successful vaginal intercourse. This percentage increased to 71.7% (38 out of 53) if only those patients who had had a BNS approach are considered. Moreover, at the 3 years follow-up assessment, 31 out of 43 (72%) patients who returned the questionnaires were still using sildenafil citrate for sexual intercourse, with a variable degree of partial erections. Interestingly, when the responses were stratified according to the neurovascular bundle status, the magnitude of improvement in SHIM score over time was greater in the BNS group than in the unilateral nerve-sparing and non-nerve-sparing groups. Significant erectile improvement was also reported combining sildenafil citrate 100 mg (taken 1–2 hours before VCD use for sexual intercourse) with VCD in men affected by ED after radical prostatectomy unsatisfied with the results of the VCD alone.[65] Indeed, this combination regimen allowed for significant erectile improvement and sexual satisfaction in 77% of the patients (24/31); furthermore, addition of sildenafil was associated with a significant increase in penile axial rigidity, as reported by both patients and their partners. Moreover, 30% (7/24) of the patients responding to this combination treatment reported a return of natural erections at 18-month follow-up. Vardenafil has been tested in patients treated with ED following unilateral or bilateral nerve-sparing prostatectomy in a multicenter, prospective, placebo-controlled, randomized study done in the USA and Canada. This was a 12-week parallel arm study comparing placebo with vardenafil 10 and 20 mg. In this study, sildenafil failures were excluded: 71% and 60% of patients treated with a BNS procedure reported an improvement of erectile function following the administration of vardenafil 20 mg and 10 mg, respectively. A positive answer to Sexual Encounter Profile (SEP)-2 question (Were you able to insert your penis into your partner's vagina?) was seen in 47% and 48% of patients using vardenafil 10 and 20 mg, respectively. A positive answer to the more challenging SEP-3 question (Did your erections last enough to have successful intercourse?) was seen in 37% and 34% of patients using vardenafil 10 and 20 mg, respectively.[66] Recently, an extended analysis focusing on the others domain of the IIEF of the same patients undergoing nerve-sparing radical retropubic prostatectomy has underlined how vardenafil was significantly superior to placebo also regarding intercourse satisfaction, hardness of erection, orgasmic function, and overall satisfaction with sexual experience ($p < 0.0009$ vs placebo for each of the variables studied) both at 10 and 20 mg doses.[67] Tadalafil was also evaluated in a large multicenter trial conducted in Europe and in the USA involving patients with erectile dysfunction following a BNS procedure: 71% of patients treated with tadalafil 20 mg reported an improvement in their erectile function compared with 24% of those treated with placebo (p <0.001). The erectile function domain score of the IIEF was significantly higher after treatment with tadalafil 20 mg compared with placebo (21.0 vs 15.2; p <0.001) and this difference was clinically significant.[12] Tadalafil 20 mg enabled a 52% rate of successful intercourse attempts to be achieved, which was significantly higher than the 26% obtained with a placebo (p <0.001).[68] The adverse-event profile of the three PDE5-I has been very similar also in this patient population and the authors of this review feel that discontinuation of treatment with one of the PDE5-I is usually caused by lack of efficacy, whereas tolerability is overall more than satisfactory.

Other medical treatments

Patients either non-responding to or who cannot use PDE5-I are typical candidates for second-line pharmacological treatment, which currently includes the intraurethral and the intracorporeal administration of alprostadil. The most recent information on the use of intraurethral alprostadil suggests that its combination with oral sildenafil may salvage a significant proportion of sildenafil failures.[69,70] Long-term efficacy and compliance data regarding intraurethral alprostadil as a treatment for post-prostatectomy ED showed that this therapy was effective in 55% of treated patients, with a drug compliance rate of 63% at mean follow-up of 2.3 ± 1.2 years after surgery. Furthermore, intraurethral alprostadil was associated with a significant increase of mean score of the SHIM compared with the preoperative period, in all men enrolled treated either with a nerve-sparing or non-nerve-sparing procedure. Better results in terms of treatment-induced erections were reported in patients with partially maintained erectile function after surgery (SHIM score ≥16).[71] Intracorporeal injection therapy with alprostadil is effective in the majority of post-prostatectomy patients, regardless of the status of their cavernosal nerves. Recently, Gontero et al have shown that the best clinical and hemodynamic response with alprostadil injection therapy is seen 1 month after the procedure, but that the attrition rate for this approach is higher when it is started at least 3 months after surgery. They proposed that in order to optimize long-term success with intracavernous injections of alprostadil, this treatment should be started 3 months after surgery, as a reasonable compromise between effectiveness and patient compliance.[72] In the experience of the authors of this review, the use of alprostadil monotherapy should be matched against the use of the combination of alprostadil, papaverine, and phentolamine. Patients treated with the three-drug combination obtain very high response rates while reporting penile pain, the typical adverse event related to alprostadil, only rarely.[73] The major disadvantage of the use of the three-drug combination is caused by its non-availability on the market, which obliges the urologist to prepare the solution on his own and then distribute it to the patient. This off-label use requires the approval of the Ethics Committee of the hospital and a signed informed consent from the patient. In a retrospective study conducted by Raina et al, 102 patients using intracorporeal injections for ED following radical prostatectomy, were assessed by means of preoperative and postoperative SHIM administration a mean of 4 ± 2.2 years after surgery.[74] Of these 102 patients, 40 had a bilateral nerve sparing, 19 had a unilateral nerve-sparing procedure, and 43 had a non-nerve-sparing procedure. Injection therapy, based on the use of either PGE_1 alone (10 or 20 μg/ml in normal saline) (61%), high-dose (20 μg/ml PGE_1 + 1 μg/ml phentolamine

+ 30 µg/ml papaverine) (19%) or low-dose triple therapy (5.88 µg/ml PGE_1 + 0.59 µg/ml phentolamine + 17.65 µg/ml papaverine) (20%), was started a mean of 9 months (range: 6–12 months) after the surgical procedure. Overall, 68% (69/102) of the patients achieved and maintained an erection sufficient for sexual intercourse and 48% (49/102) of the patients continued a long-term therapy. This excellent long-term efficacy, despite the type of intracavernosal compound used, has also been associated with a high compliance, which reached up to 70% of the patients. Although no statistically significant differences have been reported among the three-drug formulation, no mention has been made by the authors regarding eventual differences in local or systemic side effects. The same authors recently published an extended long-term analysis aimed to assess the potential successful use of open-label sildenafil citrate in men affected by post-prostatectomy ED who had been treated for a mean of 3.7 ± 1.9 years with intracavernosal agents, either PGE_1 or triple therapy (PGE_1 + phentolamine + papaverine). Overall, 41% of the patients enrolled (15/36) successfully switched to sildenafil either 50 mg (27%) or 100 mg (73%), with a higher switch rate obtained by previous PGE_1 users compared with patients consuming triple therapy, with a higher preoperative and post-intracavernosal injection SHIM score.[75]

CONCLUSIONS

Radical prostatectomy is an increasingly performed procedure in patients with prostate cancer. As the mean age of this patient subgroup is progressively declining, due to the advent of prostate cancer screening programs, the demand for optimal postoperative QoL is becoming more important. Erectile function can be preserved in patients undergoing a nerve-sparing radical prostatectomy provided that the patient is rigorously selected prior to surgery and that an anatomical radical prostatectomy following the most modern templates is precisely performed. Pharmacological prophylaxis, either with oral or intracavernosal drugs, may potentially have a significantly expanding role in the future strategies aimed at preserving postoperative erectile function.

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CHAPTER 22

Rehabilitation of continence

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INTRODUCTION

Radical prostatectomy removes the prostate together with the bladder neck sphincter mechanism and encroaches, commonly, on the upper end of the urethral sphincter mechanism. The surgeon then puts sutures through the remaining or reconstructed bladder neck and through the urethral sphincter mechanism to perform the necessary vesicourethral anastomosis to complete the procedure. With this surgically damaged and sutured reconstruction and with the inevitable postoperative edema the patient depends on his future continence. Clearly, if this process has been exacerbated by preoperative radiotherapy of any sort, to add its own toll of tissue damage, then the anastomosis and its subsequent healing will be further compromised.

Not surprisingly therefore, continence is somewhat precarious during the healing phase after surgery. For all practical purposes, most patients start off with a fairly tenuous hold on continence after a radical prostatectomy but most regain urinary control with the passage of time. The skill in managing patients after a radical prostatectomy is to recognize preoperatively when problems might occur; to recognize postoperatively when incontinence is not improving as it should; and to know when and how to intervene therapeutically.

INCIDENCE

The incidence of incontinence depends on the way in which data are collected. With a skilled surgeon and a patient with normal preoperative continence the incidence of postoperative incontinence is very low. It is certainly very low if the data on postoperative incontinence are collected by the surgeon himself.[1] With an increasing number of surgeons or institutions performing radical prostatectomy and with objective collection of data by disinterested third parties, so the incidence of incontinence increases. It also increases, or decreases, according to the definition of the term ‘incontinence’. We all know ourselves what incontinence would be if it affected us but when it affects patients the term ‘incontinence’ is used to describe everything from complete normality by anybody’s criteria to a fairly significant degree of incontinence but one which is recorded as ‘requiring only one pad per day’ in the literature. Suffice it to say that the subjective incidence of incontinence based on patient-validated questionnaires ranges from about 2% for total incontinence to about 40% of occasional leakage and occasional pad usage.[2,3]

STRUCTURE AND FUNCTION OF THE SPHINCTER MECHANISM

The key to surgical skill is an understanding of the surgical anatomy[4] (see Chapter 1). Proximally, the prostate merges with the bladder neck mechanism, which is derived from the detrusor smooth musculature. Distally, the prostate merges with the proximal element of the urethral sphincter mechanism, which it overlaps. There are three components to the urethral sphincter mechanism:

- The intrinsic smooth muscle of the urethra.
- The intrinsic striated muscle of the urethra.
- The periurethral striated muscle, derived from levator ani, which surrounds the urethra at that point.

Depending on the exact configuration of the prostate, the apex of the prostate overlaps the sphincter mechanism to some degree and is itself overlapped by striated muscle fibers that run on its surface, in some instances up to the bladder neck. The function of the urethral sphincter mechanism is not as well understood as its structure. This is mainly because the role of the urethral smooth muscle is not clear, either quantitatively or qualitatively. It is, however, recognized that it is the intrinsic striated muscle of the urethra that is the most important component as far as day-to-day continence is concerned and that the periurethral striated muscle derived from the pelvic floor is important under stress conditions but cannot compensate under normal circumstances for incompetence of the intrinsic striated muscle.[5]

The details of the innervation of these various components of the urethral sphincter mechanism are controversial[6] but it is clear that a well-performed radical prostatectomy, carefully preserving the neurovascular bundles and as much of the urethral sphincter mechanism as possible compatible with an adequate resection of the prostate, will give the best chance of postoperative continence. Whether this is simply because the best results come from the neatest possible surgery or whether there is some anatomical correlate with more than just preservation of urethral length is not clear. It seems reasonable on anatomical grounds to believe that an ‘anatomical’ radical prostatectomy will help to preserve the urethral sphincter mechanism by preserving its blood supply to the greatest possible extent; but it seems unlikely on anatomical grounds that it helps to preserve the innervation.

THE IMPORTANCE OF PREOPERATIVE BLADDER FUNCTION

It is critically important to remember that the patient’s preoperative continence is at least as important as the surgical technique of radical prostatectomy in determining postoperative continence. These days most patients presenting for radical prostatectomy tend to have T1c or T2 disease, detected by screening for prostate cancer, or otherwise low stage and early disease. Such patients commonly have no symptoms or minimal symptoms. Those with high-pressure bladder outflow obstruction due to an associated element of benign prostatic hyperplasia and those with overt bladder overactivity, common at the time of presentation 20 years ago but less common today, are an altogether different proposition, whatever the stage or grade of the prostate cancer. High-pressure bladder outflow obstruction is of course relieved by radical prostatectomy but the bladder still has to recover postoperatively and this recovery takes significantly longer than it does in a patient with asymptomatic T1c disease. Patients with uninhibited detrusor contractions may never (re)gain continence after radical prostatectomy if the uninhibited contractions continue unabated. Hence the importance of a detailed history of a patient's preoperative urinary tract symptomatology in the evaluation of postoperative incontinence.

PREOPERATIVE COUNSELING ABOUT POSTOPERATIVE CONTINENCE

In counseling patients before a radical prostatectomy, it is therefore important to point out to them that they will be losing one of their two urinary sphincter mechanisms together with part, at least, of the other. They should expect their urinary control to be less than perfect for the first few days and weeks; indeed, it might take months to return to normal but there is every likelihood that it will do so in an uncomplicated situation. A patient with overt bladder outflow obstruction, as demonstrated by a low urinary flow rate, may well take a little bit longer and suffer a little bit more in the meantime. A patient with overt bladder overactivity and frequency, urgency, and urge incontinence can well expect to have a difficult postoperative course and may never recover his continence. Likewise, the elderly or the patient with any other predisposition to incontinence should be similarly counseled. Counseling aside, there doesn't appear to be anything particular to be done preoperatively to prepare the patient for the postoperative period and to make his recovery smoother.

THE RADICAL PROSTATECTOMY WITH POSTOPERATIVE CONTINENCE IN MIND

An anatomical radical prostatectomy as described by numerous experts, but perhaps best illustrated by Walsh at the macroscopic level[7] and by Myers at the microscopic level,[8] should be advised.

Particular care is necessary in certain groups of patients according to the approach. The obvious example is the obese patient on whom it is more difficult to perform an open radical prostatectomy than a laparoscopic or robotic radical prostatectomy. Whatever the approach, of particular note is the patient with a very large prostate who will therefore have a more than usually long defect to bridge in bringing the bladder neck together with the urethra for the vesicourethral anastomosis. The anastomosis will be more prone to ischemic damage and subsequent problems, including incontinence and stricture as a consequence.

When the catheter is removed postoperatively, the patient should be expected to have a degree of frequency and urgency and probably some urge incontinence to start off with. Patients should be encouraged that once they are fully returned to normal activity, their frequency and urgency will have improved, although the incontinence may be slower to improve and a degree of stress incontinence may be found once they start to resume their normal activity. This will normally be controlled by a pad. They should be advised that most of this improvement will be in the first 2 weeks or so but that it might take 2 months or so to return entirely to normal and, indeed, it may continue to improve for up to a year.

POSTOPERATIVE FOLLOW-UP

By the time patients have been for their first routine follow-up they should be able to say that they are improving. If they are not improving within a few weeks of surgery, but they have no preoperative history of bladder symptoms, then gentle encouragement may still be all that is necessary unless the patient is unduly anxious. For the anxious patient and for those with a history of preoperative bladder outflow obstruction or bladder overactivity, anticholinergic medication with a drug such as oxybutynin or tolterodine might be helpful. Indeed, we would be inclined to prescribe one or other of these drugs prophylactically in a patient with preoperative lower urinary tract symptoms. In this age group the long-acting preparations are probably more helpful that the short-acting preparations and tolterodine (Detrusitol XL) 4 mg daily is our preferred option. If the patient has total incontinence at this stage, which is very unusual, this may suggest sphincter damage but it may nonetheless be due to the combination of a weak sphincter and an edematous anastomosis coupled with a degree of bladder overactivity and the surgeon can still be relatively optimistic. Pelvic floor exercises might be helpful in this situation. Some surgeons might advocate routine pelvic floor exercise postoperatively and certainly this has never done anybody any harm, however, there is no evidence based utility for pelvic floor exercise.

It is usually clear by 3–6 months which way things are going. The patient is either well on the way back to normality or else clearly has a persistent problem. If there were no preoperative symptoms and the patient is totally incontinent, it is likely that he has sphincter damage and that this is not going to return to normal. At this stage, urodynamic evaluation is valuable, not so much to prove the presence of sphincter weakness but to exclude outflow obstruction or detrusor overactivity. It is important to remember, also, that a patient who has a damaged sphincter as a result of a technical mishap or an ischemic anastomosis or (worst of all) preoperative radiotherapy is also likely to have an anastomotic stricture that may cause problems in its own right.[9] The more severe anastomotic strictures are typically associated with radiotherapy and salvage surgery, or radiotherapy alone, but incontinence is such a distressing symptom that it is easy to overlook an anastomotic stricture/contracture unless it is particularly severe as the symptoms of that are much less distressing. Suffice it to say that in addition to video urodynamic evaluation and a detailed pre- and postoperative assessment of symptoms, a cystoscopy is a valuable diagnostic adjunct.

If the patient has mild symptoms, it is probably worth persevering for up to a year with encouragement, pelvic floor exercise, and anticholinergic medication. For those with total incontinence beyond 3–6 months it is probably best to go for a full and accurate diagnosis and proceed to treatment.

TREATMENT OF ESTABLISHED SPHINCTER WEAKNESS INCONTINENCE

There are a number of treatments that are available, assuming the patient has proven uncomplicated sphincter weakness incontinence. For those patients with detrusor overactivity, treatment will be altogether different, and if anticholinergic medication has failed, then, these days, Botox is probably the next line of treatment that should be considered in a relatively young and relatively active man.

For sphincter weakness, the alternative treatments that have been advocated are periurethral injections, periurethral slings, and the artificial urinary sphincter.

The initial periurethral injection was Teflon.[10] This fell out of favor because the Teflon was found to ‘metastasize’. More recently collagen[11] and Macroplastique[12] have been advocated. In our experience these are rarely effective and sometimes actually make patients worse rather than better. There is an argument that minor symptoms might warrant minor treatment and that Macroplastique may therefore have a role. We do not subscribe to this point of view because of the risk of making matters worse.

Another alternative that has been suggested recently for relatively minor incontinence is the male periurethral sling.[13] This is also ineffective as far as we are concerned, and the same argument applies as with periurethral Macroplastique.[14] If a patient has incontinence severe enough to consider surgery, the only form of treatment that is effective is the implantation of an artificial urinary sphincter.[15] Implantation of an artificial urinary sphincter is not a major surgical undertaking for a patient who is fit enough to have undergone a radical prostatectomy and it is in this group of patients that the artificial sphincter has its highest efficacy and its lowest complication rate.[16] The technique is straightforward and routine now, after 25 years of usage, but is best conducted by a skilled surgeon with the appropriate experience (as is, of course, the radical prostatectomy). This implantation procedure is discussed in detail elsewhere.[17] There are only three significant problems associated with artificial sphincter implantation: infection/erosion, device malfunction and associated detrusor dysfunction.[17]

Infection/erosion, which is comparatively uncommon in patients with post-radical prostatectomy incontinence who have a device implanted, occurs in only about 4%. The infection almost always occurs at the time of implantation and is kept to the bare minimum – the same sort of incidence as is found with every other sort of surgical implant – by appropriate perioperative antibiotic treatment and the usual sterile precautions.

Malfunction with the artificial urinary sphincter is a long-term complication. It can occur early but it is unusual before 3 or 4 years after implantation and increases at the rate of about 3 or 4% per year there afterwards. At 10 years, the majority of patients still have a device implanted.

Detrusor dysfunction is not a consequence of implanting one of these devices but a coincidental problem in some of these patients, as mentioned many times already. The presence of bladder overactivity is not a bar to sphincter implantation but sphincter implantation will not cure detrusor dysfunction. If a patient has complete incontinence following a radical prostatectomy, but he had frequency, urgency, and urge incontinence preoperatively, implantation of an artificial urinary sphincter will restore him to the situation he had before his prostatectomy – i.e. with frequency, urgency, and urge incontinence (but dry between times) – which may or may not be amenable to anticholinergic medication. With sensible counseling, a patient may decide that to return to that circumstance is not of particular benefit and that he is better off with either pads or a condom drainage device to keep him dry. However, he may decide that the complete incontinence and the use of a condom drainage device is sufficiently problematic that he is inclined to accept a partial improvement with implantation of an artificial urinary sphincter, particularly if he can manage his lifestyle to achieve social continence, and, of course, if anticholinergic medication is helpful. The same consideration applies to patients with a combination of sphincter weakness incontinence and an anastomotic stricture. The presence of the anastomotic stricture is not a bar to treatment of the sphincter weakness incontinence but requires treatment in its own right – usually by instrumentation or transurethral resection to control the anastomotic stenosis/contracture/stricture (depending on your preferred terminology) before proceeding to implant the artificial sphincter.

In short, if a patient with post-prostatectomy incontinence is completely incontinent 3–6 months after his operation and has no history of preoperative bladder overactivity, he will almost certainly need and should certainly be considered for implantation of an artificial sphincter. If a patient is being considered for radical prostatectomy and has clinically overt bladder outflow obstruction or detrusor overactivity, he should be warned that he may have a degree of postoperative incontinence that would significantly impair his quality of life and that he should seriously consider some other form of treatment for his prostate cancer for this reason alone. These considerations aside, the majority of patients can expect to have problems to start off with but should recover more or less completely with time, requiring only encouragement and support during the early days when continence is precarious.

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CHAPTER 23

Oncological management after radical prostatectomy

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After radical prostatectomy, determination of cancer outcome is primarily based on measurement of serum prostate-specific antigen (PSA) level. Traditionally, the expectation is that complete removal of all prostate tissue, and cancer, results in an undetectable PSA. Thus, an undetectable PSA is assumed to represent cancer 'cure', whereas any PSA elevation is assumed to indicate failure of treatment and recurrent disease. This paradigm and discrimination has been thought to be an advantage of surgery for prostate cancer compared with radiation therapy, where precise definitions of treatment failure remain a matter of debate and uncertainty.

PROSTATE-SPECIFIC ANTIGEN

The serine protease PSA is primarily produced by prostate epithelial cells and secreted in high concentrations into the seminal fluid, although other non-prostatic tissues such as the periurethral glands may produce PSA.[1,2] Most PSA is complexed to α_1-antichymotrypsin and α_2-macroglobulin and is thought to be cleared through the liver, whereas free or unbound PSA may be cleared via the kidneys.[3,4] As a result, the true half-life of PSA is partially dependent on the free-to-total ratio. In general, the serum half-life of PSA after removal of all prostatic tissue is 2–3 days, but the free PSA component may have a significantly shorter half-life of 2–3 hours. Several weeks are required for maximal clearance of PSA and initial testing should be performed 3–4 weeks after surgery.

It should be noted that a variety of PSA immunoassays are commercially available and may yield significant intermethod variability in total measured PSA. Nevertheless, the detection limit of the assay needs to be considered in postoperative monitoring. First-generation PSA assays typically had a detection limit of 0.5 ng/ml, with subsequent improvements down to 0.05 ng/ml. Third-generation assays may have the ability to detect PSA at concentrations of 0.003 ng/ml but the clinical utility of these ultrasensitive or hypersensitive tests is unproven.[5] Patients with detectable PSA levels within a clinically relevant range (≥0.1 ng/ml) should have it repeated using the same assay to confirm this finding. Despite the numerous tests available and uncertain impact of lead time provided by newer assays, serial monitoring of post-surgical PSA remains the most effective and sensitive method of identifying persistent or recurrent cancer.

DEFINING BIOCHEMICAL FAILURE

Studies have attempted to define a clinically meaningful threshold for PSA recurrence after surgery, in order to both provide prognostic information as well as to select patients appropriate for secondary treatments. Amling et al analyzed the outcomes of 2782 men with clinically localized prostate cancer undergoing radical prostatectomy.[6] Various PSA cut points were tested to determine which value predicted continued increases in PSA as well as development of clinical disease. The 3-year risk of increasing PSA in those with PSA values >0.2 ng/ml was only 49%, whereas a significantly greater risk of 72% was associated with PSA >0.4 ng/ml; therefore, they proposed that a cut point of 0.4 ng/ml was the most appropriate definition of failure after prostatectomy. In contrast, Freedland et al found that a postoperative PSA >0.2 ng/ml was associated with a significant risk of developing additional increases in PSA.[7] Once the PSA level exceeded 0.2 ng/ml, the 1- and 3-year risk of additional increases in PSA was 86% and 100%, respectively. Thus, the most common biochemical definitions of failure include two consecutive PSA values ≥0.2 ng/ml or a single value of 0.4 ng/ml. More recently, Shen et al examined the utility of the ultrasensitive serum PSA in predicting relapse after surgery.[8] Overall, 10% of men had biochemical relapse and the ultrasensitive PSA nadir predicted the risk of early biochemical failure, defined as two consecutive PSA values ≥0.1 ng/ml. Men with a nadir <0.01 ng/ml had a significantly lower rate of relapse (4%) compared with nadir cut points of 0.01, 0.02, and ≥0.04 ng/ml, with rates of 12%, 16%, and 89%, respectively. Other studies have suggested that use of ultrasensitive PSA assays detect recurrent disease 10–22 months earlier than with conventional assays.[9,10] Additional follow-up is necessary to clarify the clinical significance of these observations and whether the natural history can be affected by earlier therapy.

Stephenson et al considered 10 definitions of biochemical recurrence after surgery and tested their association with metastatic progression.[11] Using a goodness-of-fit statistic, a PSA ≥0.4 ng/ml followed by another increase best explained metastatic progression ($R^2 = 0.21$). In addition, this threshold was associated with subsequent PSA progression, second treatment, and shorter PSA doubling time (PSA-DT). In general, definitions that required rising PSA values of at least 0.2 ng/ml performed fairly well.

RISK FACTORS FOR BIOCHEMICAL FAILURE

The assessment of risk factors for disease recurrence must be considered along with evidence of biochemical failure. Several pathological features are significant and independent predictors of disease recurrence in men undergoing prostatectomy (Table 23.1). The impact of positive surgical margins has been an area of interest and controversy, given this finding in 10–48% of surgical specimens. In a large multi-institutional analysis of nearly 6000 patients, a positive surgical margin was an important predictor of biochemical recurrence, with a hazard ratio (HR) of 3.66 ($p \le 0.001$).[12] In addition, an interaction was identified between surgical margin status and adverse pathological features, namely Gleason score 7–10 and lymph node metastasis. This further stresses the importance of obtaining negative surgical margins in patients with higher-risk disease, where the adverse effect of a positive surgical margin on prognosis is amplified.

In order to reduce the risk of biochemical failure after prostatectomy, adjuvant radiation therapy has been applied in patients with significant risk of relapse. Results from EORTC 22911 confirm the benefits of this strategy, with improvement in biochemical progression-free survival after immediate irradiation in men with positive surgical margin or pT3 disease,

Table 23.1 Predictors of biochemical recurrence after radical prostatectomy

Clinical and pathological parameter	*Relative risk (95% confidence interval)*	*p-value*
Clinical stage		0.15
Biopsy Gleason score		0.12
Specimen Gleason score:		0.0008
2–4 vs 5–6	2.48 (1.34–4.58)	0.0038
5–6 vs 7	2.48 (1.34–4.58)	0.0038
5–6 vs 8–10	4.55 (2.19–9.42)	<0.0001
Extracapsular extension:		0.0019
Focal vs none	2.17 (1.20–3.92)	0.011
Established vs none	2.72 (1.56–4.74)	0.0004
Focal vs established		0.13
Surgical margin:		
Positive vs negative	4.37 (2.90–6.58)	<0.0001
Seminal vesicle involvement:		
Present vs absent	2.61 (1.70–4.01)	<0.0001
Lymph node metastases:		
Present vs absent	3.31 (2.11–5.20)	<0.0001

Adapted from Hull et al,[50] with permission.

compared with observation after surgery.[13] Clinical progression-free survival was also significantly improved after immediate radiotherapy delivered at 60 Gy. Nevertheless, the optimal timing of radiation therapy after prostatectomy remains unclear. Nudell et al determined that outcomes in men receiving radiation therapy for biochemical failure when PSA was <1.0 ng/ml were similar to those receiving immediate adjuvant radiation therapy.[14] Similarly, the report from Stephenson et al demonstrated that salvage radiotherapy can be effective when given earlier, defined as PSA ≤2.0 ng/ml.[15] It is important to note that even men with high-risk disease characteristics, including Gleason score 8–10 or rapid PSA-DT, may exhibit a durable response to radiation therapy given after PSA relapse. A decision analysis focused on this issue suggested that only a subset of men with positive surgical margins after radical prostatectomy benefit from immediate radiation therapy, including those men with low- to intermediate-grade disease, absence of seminal vesicle invasion, and multiple positive margins.[16]

Stephenson et al developed a postoperative nomogram to predict the 10-year probability of prostate cancer recurrence after prostatectomy.[17] Significant variables included PSA, primary and secondary Gleason grade, extracapsular extension, positive surgical margin, seminal vesicle invasion, lymph node involvement, treatment year, and adjuvant radiotherapy. In contrast to previous models, this updated version extended the prognosis out to a decade as well as incorporating the use of adjuvant radiation therapy, year of surgery, and disease-free interval that the patient has achieved. The model was validated in independent data sets, with concordance indices of 0.81 and 0.79.

NATURAL HISTORY OF BIOCHEMICAL RECURRENCE

Although it is assumed that a detectable PSA after radical prostatectomy represents persistent or recurrent cancer, it is clear that the natural history of biochemical recurrence can be variable and prolonged. Pound et al characterized a cohort of 304 men with biochemical recurrence (PSA ≥0.2 ng/ml) after radical prostatectomy that was observed expectantly.[18] The median actuarial time to development of metastases was 8 years and death from prostate cancer occurred 5 years thereafter. Predictors of developing metastatic disease included time to biochemical failure, Gleason score, and PSA-DT. A subsequent update on this series confirms the potentially protracted course in men with PSA failure only.[19] The median prostate cancer-specific survival has not been reached after 16 years of follow-up and 17% of men have died from prostate cancer. Factors associated with prostate cancer-specific mortality included PSA-DT (<3 months), Gleason score (8–10), and time from surgery to biochemical recurrence (≤3 years).

Rogers et al recently described the outcomes in men failing to achieve an undetectable PSA after surgery.[20] In the group of 160 men with PSA nadir ≥0.1 ng/ml after prostatectomy, the probability of distant metastasis-free survival was 68%, 49%, and 22% at 3 years, 5 years, and 10 years, respectively. The median time to development of distant disease was 5 years. Patients could be stratified into risk groups based on specimen Gleason score, seminal vesicle invasion, and lymph node status. In addition, the PSA kinetics was an important parameter, with a PSA slope from 3 to 12 months after surgery ≥0.05 ng/ml a significant predictor of disease progression (HR = 2.9).

The potential role and significance of residual benign prostate tissue after prostatectomy has been discussed with respect to detectable postoperative PSA levels. The degree of PSA elevation due to benign glands, and incidence of this entity, remains unclear. Although it is possible that persistent PSA levels or development of low PSA values after surgery may be due to retained benign prostate tissue, it is thought that this plays a minor role when PSA reaches 0.2 ng/ml or 0.4 ng/ml. Fowler et al examined findings from anastomotic biopsies in 62 men with progressive elevation of postoperative PSA ≥0.4 ng/ml.[21] Prostate adenocarcinoma was ultimately confirmed in 92% of patients. However, in 6 cases, benign prostate tissue only was recovered from the biopsy specimens. Kernek et al addressed this issue by examining the surgical margins of prostatectomy specimens for the presence of benign prostatic tissue.[22] Of 199 prostatectomy specimens, 55 cases had evidence of benign prostatic glandular tissue at the surgical margin. This finding was not significantly associated with clinical or pathological features such as PSA, tumor volume, and pathological stage. Moreover, the presence of benign tissue at the surgical margin did not correlate with increased risk of PSA recurrence. Further research is needed on this issue to determine whether benign residual tissue could translate into detectable PSA levels using contemporary, hypersensitive assays.

EVALUATION OF BIOCHEMICAL RECURRENCE

It is estimated that as many as 50 000 men per year in the USA may develop PSA-only recurrence.[23] A study by Ward and colleagues determined that 27% of the patients who eventually develop a biochemical failure do so ≥5 years post-surgery.[24] In patients who develop biochemical failure, it appears that PSA-DT may be the best clinical predictor of death from prostate cancer.[25,26] Biochemical failure predates clinical evidence of disease and therefore may represent local failure, distant failure, or a combination of the two.[27] A clinical dilemma exists in identifying or predicting the source of the biochemical recurrence (local vs distant), as such knowledge would greatly influence the role of salvage or second-line treatment. It is also very likely that by the time clinical evidence of the disease recurrence site exists, the window of opportunity for salvage therapy may have been missed.

The natural history of prostate cancer and post-surgical biochemical recurrence was described in the landmark paper by Pound and colleagues[28] and recently updated by Freedland and colleagues.[19] That update demonstrated that an interval from surgery to biochemical failure of <3 years, a PSA-DT of <10 months, and prostatectomy Gleason score ≥8 were significantly associated with time to metastasis and prostate cancer-specific mortality. Additionally, it has been shown that pretreatment PSA kinetics may play a role in identifying patients at greatest risk for prostate cancer-specific mortality.[29] Lee and D'Amico have outlined selection criteria for men likely to benefit from salvage local therapy[27] (Table 23.2).

Table 23.2 Selection criteria for men likely to benefit from salvage local therapy

Pretreatment evidence of low-risk disease:
- Diagnostic PSA <10 ng/ml
- Clinical stage ≤T2a
- Biopsy Gleason score ≤7
- Prediagnosis PSA velocity <2 ng/ml/year

Pathological factors:
- Prostatectomy Gleason score ≤7
- Positive surgical margins
- Negative lymph nodes
- Negative seminal vesicles

Favorable post-treatment PSA kinetics:
- Interval to PSA failure >3 years
- PSA-DT >12 months
- Low absolute PSA level (<1 ng/ml)

Patient longevity:
- >10 years independent of prostate cancer diagnosis

Adapted from Lee and D'Amico,[27] with permission.
PSA-DT, prostate-specific antigen doubling time.

Another tool for determining local recurrence is transrectal ultrasound (TRUS)-guided biopsy of the prostatic fossa. Some authors have raised concern over the lack of specificity of prostatic fossa biopsies. Naya and colleagues recently reviewed the results of 100 men at a single institution who underwent TRUS-guided biopsy of the prostatic fossa without prior adjuvant therapy.[30] Twenty-nine percent of the patients in this series had a documented local recurrence. Sensitivity and specificity values for TRUS biopsy and digital rectal examination (DRE) were compared: DRE had a sensitivity of 72.4% and a specificity of 64.8%; the corresponding values for TRUS biopsy were 86.2% and 53.5%, respectively. Multivariate analysis showed abnormal TRUS findings and PSA concentration at biopsy to be independent predictors of positive fossa biopsy results. No men in their series with PSA <0.5 ng/ml, normal TRUS, and normal DRE had positive fossa biopsy. Koppie et al reviewed the role of anastomotic biopsy findings in predicting outcomes after radiotherapy following radical prostatectomy.[31] They studied 67 patients who received radiotherapy for biochemical- ($n = 33$ patients) or biopsy-proven ($n = 34$ patients) recurrent prostate cancer following radical prostatectomy. There was no significant difference in biochemical recurrence-free survival between these two groups, and thus the authors concluded that a positive anastomotic biopsy did not predict for an improved outcome in patients receiving radiotherapy following radical prostatectomy.

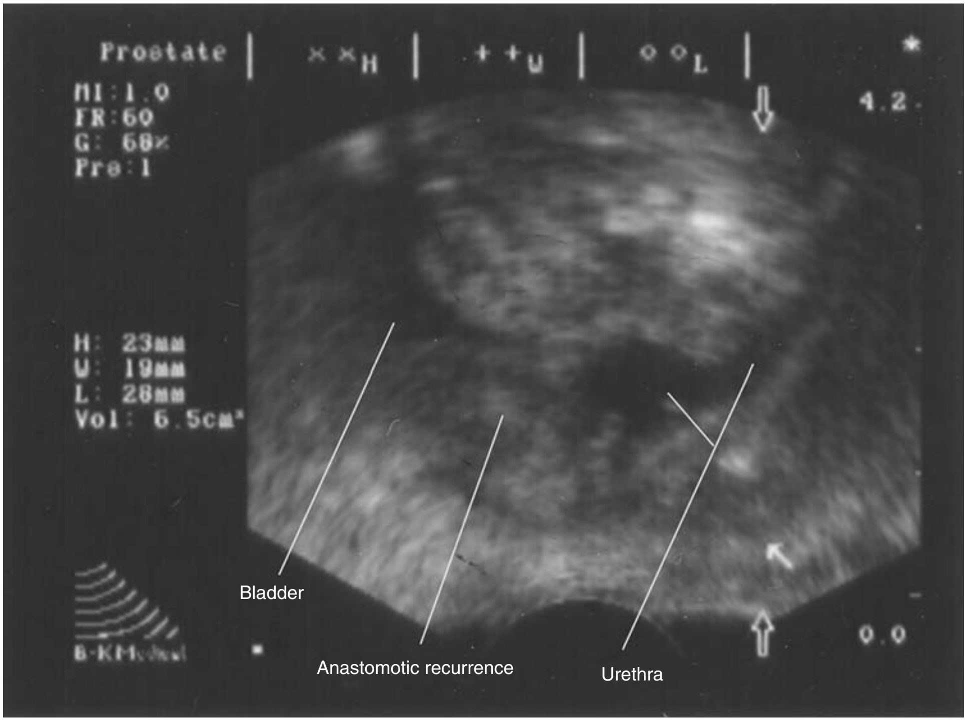

Figure 23.1 Transrectal ultrasound (sagittal view) of a patient with a rising prostate-specific antigen (PSA) level post-radical prostatectomy. The mass is suspicious for local recurrence at the site of the anastomosis, and biopsy was positive for prostate cancer.

We do believe that TRUS of the prostatic fossa (Figure 23.1) may be particularly helpful for patients who will be receiving radiotherapy following radical prostatectomy, as it provides a vector for image-guided placement of gold seeds to serve as fiduciary markers for real-time, online portal imaging during radiation therapy treatment session.

The most common site of distant recurrence of prostate cancer is bone, and the imaging study of choice for detecting bony metastasis is the technetium 99m methylene diphosphonate bone scan. The clinical trigger for performing a bone scan in the post-radical prostatectomy patient has been the PSA level. In 1991, Terris and colleagues recommended bone scans be performed when the postoperative PSA level became detectable.[32] Since then, others have suggested that the likelihood of a positive bone scan in the postoperative patient is <5% until the PSA reaches 40 ng/ml.[33] More recently, Kane and colleagues have demonstrated that for a PSA recurrence <10 ng/ml, only 4.5% of patients had a positive bone scan.[34] Recently, Dotan and colleagues have developed a nomogram that combines preoperative and postoperative parameters to predict the probability of having a positive bone scan.[35] The authors of this nomogram achieved a concordance index of 0.93, suggesting a highly accurate predictive model. Nomograms such as this one may potentially spare the patient and the healthcare system many unnecessary bone scans by helping to eliminate unnecessary scans.

The ^{111}In-capromab pendetide (ProstaScint) scan is a nuclear medicine study based on a murine monoclonal antibody to an intracellular component of prostate-specific membrane antigen (PSMA); the antibody is conjugated to ^{111}indium.[36] In the post-radical prostatectomy patient, the ability of ^{111}In-capromab pendetide radioimmunoscintigraphy to detect prostatic fossa recurrences has had low sensitivity and specificity, creating debate over its clinical utility in this context.[37] More promise may lie in ^{111}In-capromab pendetide radioimmunoscintigraphy's ability to rule out extraprostatic fossa sites of recurrence.[37] Others have argued that ^{111}In-capromab pendetide radioimmunoscintigraphy may be more sensitive than computed tomography (CT) scan or bone scan for identifying recurrent disease in patients with low PSA levels.[38] In general, it is considered not very useful for detecting local recurrence.[39] Emerging evidence suggests that newer antibodies which target the extracellular domain of PSMA may provide significant benefits for prostate cancer imaging.[40] Bander and colleagues reported the first clinical studies of one such antibody, mAb J591, the first monoclonal antibody to the extracellular domain of PSMA tested in patients (Figure 23.2).[41]

TIMING AND TYPE OF ANDROGEN ABLATION

A comprehensive discussion of the role of androgen ablation is beyond the scope of this chapter. Here we briefly review some of the more recent developments in this area. Optimal timing of androgen deprivation therapy (ADT) – whether achieved by LHRH (luteinizing hormone-releasing hormone) analogue or castration – remains unknown. Messing and colleagues reported on a series of patients who were found to have nodal metastases at the time of radical prostatectomy and showed improved survival among patients treated with early ADT.[42] At a median follow-up of 7.1 years, 7 of 47 men in the immediate ADT group had died compared with 18 of 51 in the observation group ($p = 0.02$).[42] The authors recently published a follow-up to this study, showing, at a median follow-up of 11.9 years, the men in immediate ADT group demonstrated improved overall survival (HR = 1.84, $p = 0.04$), prostate cancer-specific survival (HR = 4.09, $p = 0.0004$), and progression-free survival (HR = 3.42, $p < 0.0001$).[43] Side effects commonly observed with ADT include loss of libido, erectile dysfunction, hot flashes, gynecomastia, anemia, and osteoporosis.[44] Bicalutamide (a non-steroidal antiandrogen) is associated with maintenance of sexual interest, physical ability, and bone mineral density.[45] The ongoing Early Prostate Cancer (EPC) trial has shown at a median follow-up of 7.4 years, bicalutamide 150 mg has improved progression-free survival irrespective of standard of care.[45] However, no survival difference has been noted in the prostatectomy patient subgroup.[45] The Scandinavian Prostatic Cancer Group Study No. 6 (SPCG-6), one of three ongoing trials within the EPC program, was designed to determine the effects of bicalutamide on progression-free survival and overall survival. In the second analysis of SPCG-6 with 5.3-year median follow-up, the authors noted that in patients with localized disease, the bicalutamide group (150 mg/day) had decreased survival compared with the placebo group. There did not appear to be a particular cause of death to account for this finding.[46]

CHEMOTHERAPY AND NOVEL THERAPEUTIC APPROACHES

The advent of taxane-based chemotherapy in patients with hormone-refractory prostate cancer has shifted the role of chemotherapy in this patient population from one of improving

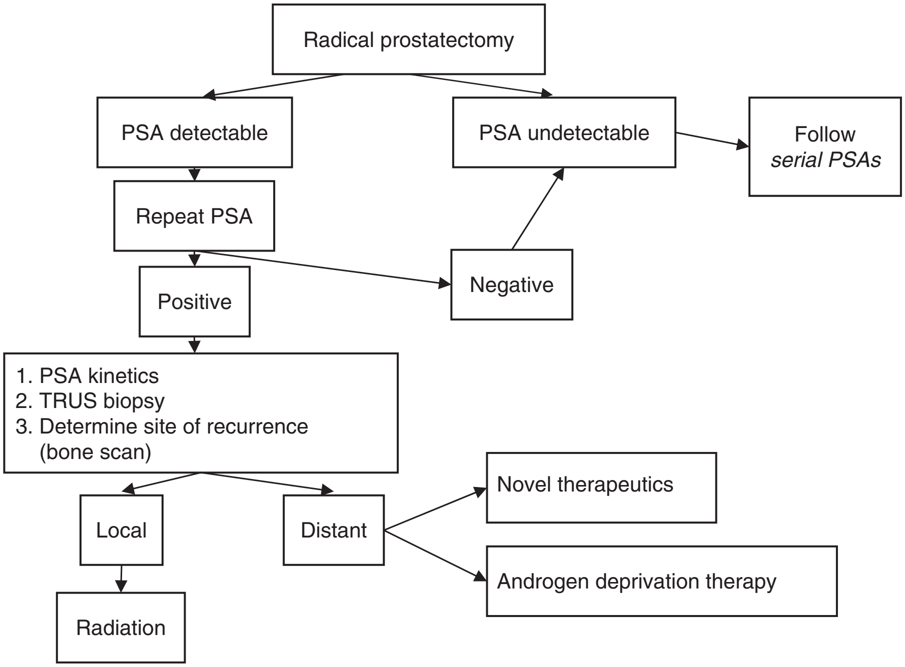

Figure 23.2 Treatment algorithm for the post-radical prostatectomy patient. PSA, prostate-specific antigen; TRUS, transrectal ultrasound.

quality of life to one of increasing survival. Two phase III randomized trials have demonstrated this survival benefit. SWOG 9916 demonstrated an 18-month median survival for patients in the combination docetaxel/estramustine group compared with 15 months for the mitoxantrone/prednisone group.[47] Similarly, TAX 327 showed the docetaxel/prednisone group to have a median survival of 18.9 months compared with 16.5 months for the mitoxantrone/prednisone group.[48] This study also demonstrated significant improvement in pain control in the docetaxel group.[48] What both these studies demonstrate is that prostate cancer should no longer be considered a chemoresistant disease.[49] Two cooperative group studies are currently underway to examine the role of neoadjuvant (CALGB 90203) and adjuvant (SWOG 9921) chemotherapy in high-risk localized prostate cancer.[49]

CONCLUSION

Over the past 25 years we have gained considerably in our understanding of the natural history of prostate cancer. Maturing data sets and well-designed clinical trials have taught us much about PSA kinetics and elucidated risk factors for biochemical failure and prostate cancer-specific mortality. The future holds great promise for the role of novel therapeutic approaches to patients with high-risk localized disease and for those with biochemical failure without evidence of clinically metastatic disease.

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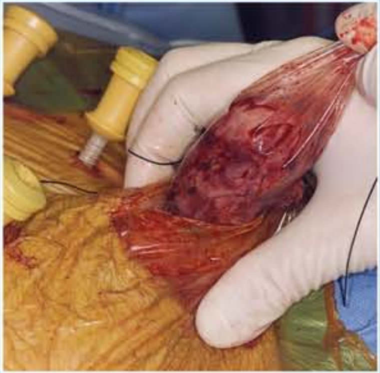
RADICAL PROSTATECTOMY:

from open to robotic



Radical prostatectomy involves the surgical removal of the entire prostate gland and the seminal vesicles. Recently the open operation has been challenged by laparoscopic and robotic techniques. However, making the transition to this new technology is not an easy option. Avoiding surgical complications such as incontinence and ensuring continued erectile function following the procedure requires good surgical technique by whatever means.

Radical Prostatectomy, with an outstanding editorial team of Roger Kirby, Francesco Montorsi, Paolo Gontero and Jay Smith, fully explores the various issues in a clear, informative and well illustrated way. Clearly split into six sections, the book features chapters on:

- Anesthesiological care during and after radical prostatectomy
- Nerve sparing radical prostatectomy
- The extraperitoneal and transperitoneal technique of laparoscopic radical reptropubic prostatectomy
- The experiences of three major institutions concerning the transition from open to robotic surgery
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